

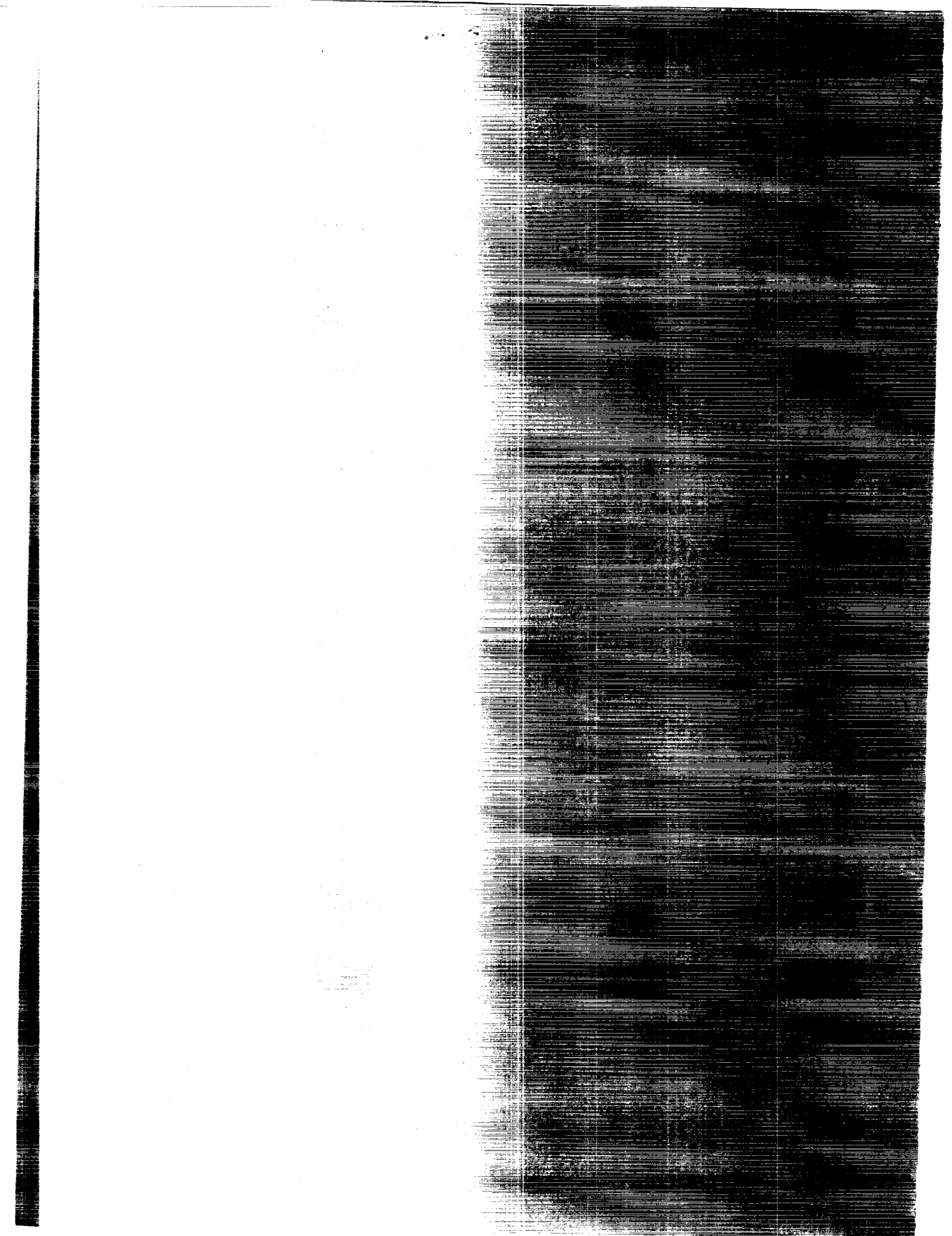
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Issue 25

Edited by

Lydia Razran Hooke and Ronald Teeter
Lockheed Engineering and Sciences Company
Washington, D.C.

Victoria Garshnek
George Washington University
Washington, D.C.

Joseph Rowe
Library of Congress
Washington, D.C.

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To our readers: We are working in a large number of highly technical, specialized areas for which adequate Russian-English glossaries have yet to be compiled. We ask your help in improving the accuracy and specificity of our English terminology. Please fill out the form below whenever you encounter an incomprehensible, incongruous, awkward or otherwise inappropriate term. While we solicit all suggestions for improved renderings, the statement that a term is inappropriate provides us with useful information, even when no better alternative can be suggested. A copy of this form will appear in all future issues of the Digest. Thank you for your help.

Abstract Number	Incorrect or inappropriate term	Suggested rendering

**PLEASE RETURN TO: Dr. Lydia Hooke
Lockheed Engineering
and Sciences Company
600 Maryland Ave. SW
Suite 600, East Wing
Washington, DC 20024**

FROM THE EDITORS

This is Issue 25 of the USSR Space Life Sciences Digest. The following abstracts deal directly with space flight data: Botany P1154 , page 3; Endocrinology P1129, page 22; Immunology P1170, page 35; Metabolism P1134, page 54; Microbiology P1135, page 63, and P1149, page 67; Nutrition P1128, page 88; Space Biology and Medicine P1152, page 93. An Index for Digest Issues 21-25 will be distributed shortly.

Address correspondence to:

Dr. Lydia Hooke
Lockheed Engineering
and Sciences Company
600 Maryland Ave. SW
Suite 600, East Wing
Washington, DC 20024
Phone (202) 863-5269

BODY FLUIDS

PAPER:

P1136(25/89)* Vartbaronov RA, Glod GD, Popov IG, Uglova NN, Sarycheva NN, Rolik IS.
Blood electrolyte balance in dogs repeatedly exposed to +G_z acceleration
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(4): 43-46; 1989.
[23 references; 7 in English]

Body Fluids, Blood Electrolyte Balance
Dogs
Acceleration, +G_z

Abstract: Experiments were performed on seven outbred dogs. +G_z acceleration was created on a centrifuge with radius of 4.5 m. For a 5-month period, the animals were regularly exposed to one to two sessions of acceleration increasing to endurance limits. In each case, acceleration was terminated when EKGs showed clear manifestations of cardiac rhythm disruption. Blood was taken for biochemical research 2-3 days after exposure to acceleration. In an additional condition, a state of hypermagnemia was created through intramuscular injection of a 25% solution of magnesium sulfate in a dose of 0.5 ml/kg. Animals' functional state here and in the acceleration condition was evaluated by recording EKGs in three standard leads. Additionally, tetrapolar thoracic impedance plethysmograms were used to obtain data on cardiac stroke volume, circulatory minute volume, and a parameter of total peripheral resistance. Blood for biochemical studies was taken from the femoral vein before and 45-50 minutes after injection. Concentrations of Na⁺ and K⁺ in plasma were measured using flame photometry, while Mg²⁺ concentration was determined by a color change with reagents, and Ca²⁺ concentration was determined using a titrometric solution of trialon B. The effect of hypermagnemia on the functional state of the myocardium and endurance of acceleration was evaluated by comparing the results of centrifugation with and without the magnesium sulfate injection.

Two weeks after the beginning of weekly exposure to acceleration, the subjects displayed hyponatremia at rest and an increased potassium/sodium ratio. After 2 months, concentration of Na⁺ returned to baseline, but stable hyperkalemia and hypermagnemia and an elevated potassium/sodium ratio were observed. Since previous data indicate that the greatest increase in endurance of acceleration occurs toward the end of the first month of regular exposure, the authors conjecture that the initial hyponatremia noted here reflects a restructuring of electrolyte balance in the process of adaptation. After 2 months of regular exposure, a new level of homeostasis was achieved involving hyperkalemia and hypermagnemia, which may have an antiarrhythmic effect under exposure to +G_z acceleration. This hypothesis is strengthened by the fact that when magnesium is injected and subjects exposed to acceleration, circulatory minute volume and endurance levels increase significantly. The authors conclude that electrolyte balance is important in adaptation to repeated acceleration and that Mg²⁺ is highly significant in compensating for disruptions of cardiac rhythm induced by acceleration. They suggest, however, that this is an indirect effect, which acts by reducing loss of intracellular potassium through increasing activity of Na-K-dependent ATPase.

Table 1: Concentrations of electrolytes in plasma of dogs in the process of systematic exposure to +G_z acceleration

Table 2: Hemodynamics, concentrations of plasma electrolytes and level of hematocrit after injection of magnesium sulfate in seven dogs

BODY FLUIDS

Table 3: Hemodynamics under exposure to +G_z acceleration and tolerance of increasing acceleration

Condition	Parameter	Heart rate, per minute	Stroke vol., ml	Cardiac out put, l/min	Total periph. resist., units	Endurance +G _z , units
Centrifuga- tion alone	Absolute	218±19.8	9.8±1.8	2.0±0.35	1.14±0.14	14.6±0.7
Centrifuga- tion 50 min after injection	Absolute	246±15.6	10.6±1.8	2.64±0.54	1.23±0.11	15.8±0.6
	Difference	28.4±14.4	0.81±0.51	0.64±0.21*	0.09±0.17	1.2±0.4*
	t	1.27	1.59	3.05	0.53	3.05
	% change	16.3±7.9	12.5±7.7	30.0±9.8*	20.0±20.7	8.7±2.5*
	t	2.07	1.62	3.06	0.27	3.4

* difference from control significant (level not specified)

BOTANY

PAPERS:

P1154 (25/89) Laurinavichyus RS, Yaroshyus AV, Rupaynen OYu.

Prospects for use of higher plants in life support systems.

In: Malkin VB, Kosmolinskiy FP, Kuznets Yel (editors).

Chelovek i Kosmos: Idei K.E. Tsiolkovskogo i ikh razvitiye v sovremennoy biomeditsine. Trudy XXII Chteniy, posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idej K.E.

Tsiolkovskogo (Kaluga, 15-18 sentyabrya 1987)

Человек и Космос Идеи К.Э. Циолковского и их Развитие в современной Биомедицине. Труды XXII Чтений; посвященных разработке научного наследия и развитию идей К.Э. Циолковского (Калуга; 15-18 сентября 1987)

Man and space: The Ideas of K.E. Tsiolkovskiy and their development in modern biomedicine. Works from the XXII lecture series devoted to development of the scientific heritage and development of the ideas of K.E. Tsiolkovskiy (Kaluga, 15-18 September, 1987)

Moscow: Soviet Academy of Sciences; 1988.

[[7 references; 1 in English]

Pages 55-60.

Botany, Development, Growth, Viability
Higher Plants, Arabidopsis, Seeds
Space Flight, Salyut-7, Life Support Systems

Abstract: This paper analyzes aberrations found in arabidopsis plants grown in the "Phyton-3" device on Salyut-7. Experimental conditions are not described, since they are presented in the authors' earlier works.

At the end of the 69-day experiment, only half the flight seeds were mature, while all the control seeds were. In the control device, eight plants grew, all of which bore normal pods with seeds. In the experimental culture, eight plants grew, two of which had sterile (seedless) pods. Analysis of subsequent generations showed that there were 42% embryonal deaths in first generation descendants of flight seeds and 22.5% deaths in the control condition. No differences were noted in the second generation, neither in embryonal deaths nor in rate of growth.

Analysis of the anatomical structures of the green leaves remaining on the stalks of plants in both groups revealed the same structural elements. On both sides, with approximately equal frequency, there were convex stomata, a system of vessels with well formed elements of xylem and phloem. The mesophyll cells contained chloroplasts. Size and number of these elements are presented in Table 2.

Table 2 shows that the number of chloroplasts in the cell and the leaf areas were approximately the same. Analysis of microphotography of ultrathin sections showed that leaves of the control and flight plants contained chloroplasts with the typical elongated shape and a well-developed membrane system. But some cells of flight plants were irregular in shape, with protuberances and invaginations in the external membrane. It was established that the mean area of the chloroplasts of flight plants was 30% less, and the perimeter 11% smaller than that of the chloroplasts of control plants. It was also noted that in the majority of cases, the control chloroplasts contained significantly more starch granules than the experimental ones. Along with chloroplasts with normal internal structure, flight plants contained plastids in which stromal labella were not aligned or were truncated. In these chloroplasts the grains were not arranged parallel to the external membrane, as is normally the case, but wound around in the form of a vortex. This orientation with respect to the long axis of the cell prevented them from being parallel to the lateral surface of the cell, which could significantly affect photosynthesis.

It should be noted that changes in the structure of chloroplasts were also noted when funaria moss and orchids were grown in space.

Space flight conditions affected the final length of the stalks of the arabidopsis: at the termination of the experiments, the mean length of experimental plants was 9.6 ± 0.48 mm, while for the control the corresponding length was 17.5 ± 1.43 mm. Differences in anatomical structure were also noted (Table 3).

To the unaided eye, the overall anatomical structure of a stalk cross-section was similar in the two groups. However, photometric analysis of individual tissues showed statistically significant differences. First, as can be seen in Table 1, the thickness of the stalk increased in space. This was primarily due to an increase in the areas of the parenchyme of the cell epidermis and primary root. In addition, cells of the parenchyme of the primary root were greater in area for flight cells, while perimeters were equivalent to those of the control group. This suggests that the cells in weightlessness became more spherical, resulting in the appearance of intercellular channels not present in control plants.

Thus, the experiment with arabidopsis plants showed that the growth and reproduction of a single generation of plants is possible under space flight conditions. However, the plants displayed significant retardation in growth and development, and changes in the anatomical structure of stalks, the morphological characteristics of chloroplasts and their ultrastructure. Although the overall productivity of space plants was not determined, it is reasonable to conclude that it would be lower than in the control, since the dimensions of the axial organs (stalk height), as well as the dimensions of seeds (0.431×0.2265 mm in the control and 0.405×0.244 mm in the experimental condition) were considerably less than in the control. This is not suitable for future life support systems where, higher rather than lower productivity will be needed. To accelerate understanding of physiological principles of space horticulture, it must be determined which space flight factors have a direct effect on the physiological processes, and which an indirect effect, mediated by physical phenomena occurring in the gas and liquid media under conditions of weightlessness. The authors recommend experiments involving centrifugation (at 1-g) of plants in space.

Table 1: List of experiments on growing higher plants in space

Table 2: Effects of space flight factors on morphological parameters of chloroplasts of arabidopsis leaves

Parameters	Control	Experimental
Number of chloroplasts in a cross-section of cells	3.93 ± 0.11	4.09 ± 0.12
Number of chloroplasts in 1 mm ² area of a cross section	8572 ± 445	8072 ± 307
Area of chloroplast	361.7 ± 15.7	$257.5 \pm 9.0^*$
Perimeter of chloroplast	78.2 ± 1.5	$69.5 \pm 1.2^*$
Length of chloroplast	31.1 ± 0.6	$27.9 \pm 0.5^*$
Width of chloroplast	14.3 ± 0.4	$11.8 \pm 0.3^*$

* intergroup difference statistically significant, $p < 0.01$

Table 3: Anatomical parameters of stalks of arabidopsis grown on the ground and in the Phyton-3 device on Salyut-7

Parameters		Control	Experimental
Cross section	area	22599±466	30345±365
	perimeter	581±7.3	653±4.3
Epidermal cells	area	74.7±1.7	109.4±2.4
	perimeter	32.5±0.4	38.7±0.4
Parenchyme cells of the primary root	area	99.4±1.7	104.5±1.4
	perimeter	38.3±0.3	38.5±0.3
Vascular bundles	area	614.2±2.7	775.7±35.0
	perimeter	103.8±2.8	123.1±4.0
Cells of the paren- chyme core	area	136.8±6.0	136.7±7.8
	perimeter	43.7±0.9	47.1±1.2

P1155(25/89) Poluyan YeS, Tikhomirov AA, Sid'ko FYa.

The role of infrared radiation in increasing the productivity of plants.

In: Malkin VB, Kosmolinskiy FP, Kuznets Yel (editors).

Chelovek i Kosmos: Idei K.E. Tsiolkovskogo i ikh razvitiye v sovremennoy biomeditsine. Trudy XXII Chtenij, posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idej K.E.

Tsiolkovskogo (Kaluga, 15-18 sentyabrya 1987)

Человек и Космос Идеи К.Э. Циолковского и их Развитие в современной биомедицине. Труды XXII Чтений; посвященных разработке научного наследия и развитию идей К.Э. Циолковского (Калуга; 15-18 сентября 1987)

Man and space: The Ideas of K.E. Tsiolkovskiy and their development in modern biomedicine. Works from the XXII lecture series devoted to development of the scientific heritage and development of the ideas of K.E. Tsiolkovskiy (Kaluga, 15-18 September, 1987) Moscow: Soviet Academy of Sciences; 1988.

[5 references; none in English]

Pages 61-64.

Botany, Productivity, Life Support Systems

Higher Plants, Radishes, Cucumber

Radiobiology, Infrared Radiation, Photosynthetically Active Radiation

Abstract: This work attempted to determine the optimal ratio of photosynthetically active radiation and infrared radiation for providing the maximum productivity and utilizable biomass under otherwise equal growth conditions. The results were intended to be used to develop optimal growth regimens for manned space flights. Subjects were radish and cucumber plants, selected because they differ in morphology and various aspects of reproductive development. Various experiments were performed in which the ratio of ultraviolet radiation was changed while the level of photosynthetically active radiation remained the same. Plants were grown in a thermostatic phytotron on keramzyte, and Knop nutritive medium. Level of photosynthetically active light was maintained at 100 W/m^2 . In different experimental conditions proportion of infrared radiation was: I - 50%; II 15%; III - 0. Conditions II and III differed only in the intensity of the infrared light, while in condition I, the spectral composition was also different, with powerful peaks in the area 800-900 nm, absent in the other infrared light used. Only close infrared with $\lambda < 1200$ was used; a fluid screen absorbed remote infrared. The radish plants were grown under conditions of continuous illumination at a temperature of $20 \pm 0.5^\circ\text{C}$. The cucumbers were grown with a 16-hour photoperiod, at a temperature of $24.0 \pm 0.5^\circ\text{C}$ and $20 \pm 0.5^\circ\text{C}$, for light and dark periods, respectively.

The experiment with the radish plants showed that the growth characteristics were significantly lower with a smaller proportion of infrared. Plant height was 2.6 times greater, leaf area 2.5 greater, and above-ground biomass 1.5 times greater in condition I than in condition II. Edible biomass increased only insignificantly. Coefficient of efficiency thus decreased as proportion of infrared increased. Infrared had an analogous effect on cucumber growth parameters. On day 30 the plants grown in 50% infrared were twice as tall as plants grown with 15%, while leaf size was greater by a factor of 1.5. Number of leaves was the same. Infrared radiation did not affect pigment concentration nor rate of gas metabolism in either plant.

Thus, although infrared radiation did not affect photosynthesis, neither did the leaves remain completely unaffected. A 15% fraction of infrared allowed cucumbers to form with reduced internodal distance, so that the proportion of fruit per unit stalk length and thus plant productivity increased. In the case of radish plants, productivity was highest in the absence of infrared. These results show that proportion of infrared can affect plant productivity in a closed system and that the most beneficial proportion may vary for individual species.

Table 1: Some characteristic of radish plants grown under varying proportions of infrared

% Infrared	Plant Height (cm)	Leaf Area (dm ²)	Root Crop Wt.(kg/m ²)	Leaf Weight (kg/m ²)	Productivity Index(%)
50%	15.5	5.02	5.35	2.99	64
15%	9.9	2.99	5.04	2.10	69
0%	6.0	2.03	4.67	1.82	72

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

PAPERS:

P1156(25/89)* Korkushko OV, Shatilo VB.

Characteristics of the transitional process of cardiac rhythm in response to a stand test in middle-aged and elderly subjects.

Fiziologiya Cheloveka.

15(4): 29-34; 1989.

[20 references; 3 in English]

Authors' Affiliation: Institute of Gerontology, USSR Academy of Medicine, Kiev

Cardiovascular and Respiratory Systems, Cardiac Rhythm

Humans, Age Differences

Stand Test, Physical Exercise; Neurophysiology, Sympathetic, Parasympathetic Nervous Systems

Abstract: The transitional process of cardiac rhythm was studied using stand tests in 122 apparently healthy subjects aged 20-34 (40 people), 60-69 (52 people), and 80-89 (30 people). An additional group consisted of 15 individuals, aged 60-69, who had engaged in a regular running program for 5-10 years. The sessions were held in the early part of the day at least 2 hours after meals. The cardiac transition period was recorded using a rhythmogram (apparently a recording cardi tachometer). First the subject lay on his back for 20 minutes and then was asked to stand rapidly and continue standing for 5-7 minutes. The transition to vertical position lasted no more than 3-5 seconds. Four points were identified on the rhythmogram: A - the value of the R-R interval while subject was recumbent, B - the minimal R-R interval in the transitional state, C - the maximal R-R interval in the transitional state, D - the R-R interval at the end of the transitional period. These four points divide the transitional period of cardiac rhythm into three phases: I - the phase of initial speeded heart rate on standing up (AB interval), B - the subsequent phase of decreasing rate (BC interval), III - the phase of gradual stabilization of heart rate in the orthostatic position (CD) interval. The following parameters were measured:

1. Amplitude of response of cardiac rhythm in the transitional period $\Delta RRB = \frac{RRA - RRB}{RRA} \times 100$
2. Amplitude of restoration of regulation: $\Delta RRC = \frac{RRC - RRB}{RRA(sic.)} \times 100$
3. Duration of phase I;
- 4 Duration of phase II;
5. Duration of entire transitional period.

To elucidate the possible role of sympathetic and parasympathetic effects, some subjects were injected with anaprilin (propranolol hydrochloride) or atropine solutions and the stand test was performed again. Blood pressure was measured in the recumbent position and in minutes 1-5 in the standing position. The three periods were clearly noted in 95% of the cases in subjects in the youngest age group. In the group aged 60-69, these three phases still predominated, but significantly more bi- (21%) and monophasic (16%) patterns were encountered. In the oldest group, 50% displayed a single period and only 30 showed all three. Physically fit individuals, aged 60-69, were more likely to show three phases and less likely to show one than others of their age. Blood pressure data indicated that the hypodynamic response to assumption of a vertical position was 2.2 times more likely to occur in middle-aged and elderly subject than in young subjects.

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

It has been considered that the parameter ΔRR_B reflects activation of the sympathetic nervous system, while ΔRR_C reflects increased parasympathetic tonus. Duration of phases I and II are related to how rapidly the sympathetic and parasympathetic nervous systems are activated. Studies using anaprilin and atropine confirmed this. Two hours after administration of anaprilin, which blocks the sympathetic nervous system, the amplitude of heart rate response decreased, phase I shortened, and phases II and III lengthened in duration. Administration of atropine had the opposite effects.

All parameters of the transitional process of cardiac response to standing are affected by age. The highest correlations with age occur with ΔRR_B ($r=-0.78$), ΔRR_C ($r= -0.82$), and duration of the entire transition ($r = +0.70$). Thus, with aging, both sympathetic and parasympathetic effects on cardiac rhythm response to standing are attenuated; however, the parasympathetic effects decrease most. Increases in temporal parameters of the transitional phase with age suggest a slowing rate of activation of both sympathetic and parasympathetic systems. Results can be attributed to the dystrophic and destructive changes occurring with age. The fact that middle-aged subjects engaging in physical training have parameters "younger" than their peers is interesting in this regard.

Table 1: Distribution of types of transitional processes of cardiac rhythm in response to the stand test in healthy individuals varying in age

Table 2: Some parameters of the transitional process of cardiac rhythm in response to the stand test in healthy individuals varying in age

Figure 1: Types of transitional process in cardiac rhythm in response to a stand test

Figure 2: Diagram of a triperiodic type of transitional process in cardiac rhythm in response to a stand test

P1157(25/80) Buzulina VP.

The effect of body position on endurance of physical exercise after long-term hypokinesia.

Fiziologiya Cheloveka.

15(5): 123-126; 1989.

[16 references; 6 in English]

Cardiovascular and Respiratory Systems, Endurance, Exercise

Humans, Males

Hypokinesia With Head-Down Tilt, Long-Term; Body Position

Abstract: Subjects in this study were 24 males (mean age 30.1). All underwent a special medical selection process and demonstrated relatively high tolerance for exercise and orthostatic tests. Subjects spent 49 days under conditions of hypokinesia with head-down tilt (-4°). The exercise test involved pedaling a bicycle ergometer at a load of 100 W and a rate of 60 revolutions per minute for 7 minutes. Each subject performed the exercise twice, once in a sitting and once in a supine position, with an interval of 2 days between the sessions. During the exercise sessions the following parameters were recorded: heart rate, oxygen consumption, exhalation of carbon dioxide, and respiratory minute volume. At rest and after attainment of a "steady state" in minute 6 of exercise, the method of rebreathing was used to determine cardiac output and compute stroke volume

In the baseline period, there was a difference between sitting and supine position at rest in heart rate, stroke volume, and respiratory minute volume. No such differences were noted when the subjects were exercising. After the hypokinesia period the majority of subjects noted a feeling of weakness, more severe when they were sitting up. After hypokinesia at rest, heart rate increased in sitting position by 29.4%, and in supine position by 14.5% compared to baseline data. Stroke volume decreased by 17% in both positions. After hypokinesia, physical exercise in a sitting position put substantially more stress on the cardiorespiratory system than before the treatment. Heart rate increased by 29.2% in subjects as a group and in eight reached submaximal values. Increased cardiac output was less pronounced in response to exercise than before treatment. Respiratory minute volume increased by 65% in response to exercise in the baseline period, and by only 33% after hypokinesia. After hypokinesia when exercise was performed in a supine position, changes analogous to those occurring in seated subjects occurred, but were less pronounced.

In the baseline period response of stroke volume was virtually the same in sitting and supine position. After hypokinesia, exercising stroke volume decreased significantly more in a sitting position.

Table: The effects of hypokinesia with head-down tilt on parameters of the cardiorespiratory system in response to exercise in sitting and supine positions

P1162(25/89) Serebrovskaya TV, Ivashkevich AA, Maydikov YuL.

The association between reactivity of the respiratory system, mental and physical work capacity and properties of metabolism in humans after a year's exposure to high altitudes.

Fiziologicheskii Zhurnal.

35(4): 61-69; 1989.

[34 references; 11 in English]

Authors' affiliation: A.A. Bogomolets Institute of Physiology, Ukrainian Academy of Sciences, Kiev

Cardiovascular and Respiratory Systems, Metabolism, Human Performance, Work Capacity,
Physical, Mental
Humans, Males, Individual Differences
Adaptation, High Altitudes

Abstract: The goal of this study was to investigate the associations among individual differences in respiratory system reactivity, mental and physical work capacity, and certain properties of metabolism in humans during a 1-year period at moderately and extremely high altitudes. Subjects were 46 apparently healthy males divided into two groups. Group 1 contained males (mean age 19.6) born at sea level, who lived for a year at an altitude of 1680 m above sea level. Group 2 contained 22 healthy males (mean age 20.8) born at sea level, who lived for a year at an altitude of 3650 m with periodic ascents to a height of 4200 m. Group 1 subjects were tested at 1680 m and group 2 subjects at 3650 m. Parameters of respiration and gas exchange at rest and during graded physical exercise were measured using traditional methods. Sensitivity to hypoxia was measured using rebreathing with absorption of CO₂ on a spiograph for approximately 4 minutes. The procedure was terminated when the subject made an error in simple arithmetic problems. Concentration of gas in alveolar air was monitored. Curves of ventilatory response were evaluated by a method allowing identification of slow increase in ventilation during the initial phase of exposure to hypoxia and the area of rapid increase in response to significant hypoxia. Physical work capacity was evaluated using PWC₁₇₀ test with two graded loads. Arterialized blood was taken from the finger at rest and during the first 15 seconds after the second exercise load (75% of required maximal oxygen consumption for 3 minutes) for study of acid-base status and carbohydrate metabolism. Parameters used to investigate the latter included concentrations of glucose, lactic acid, and pyruvic acid. Blood pH was also measured. Mental work capacity was measured by determining simple visual-motor reaction time, and reaction time to select a target stimulus with one or two distractors. Visual information processing capacity was measured using a Landolt eye chart; parameters used were speed of information processing and total information processed. Subjects provided self-ratings of functional state; and , parameters of well-being, activity, and mood were derived.

Subjects temporarily living at moderately (group 1) and extremely high (group 2) altitudes manifested both commonalities and differences. Group 2 subjects displayed hyperventilation at rest, diminished oxygen consumption, increased sensitivity of the respiratory center to the hypoxic stimulus (both first and second stages of the reaction), increased endurance ceiling for hypoxia, and decreased physical work capacity as indicated by the PRC₁₇₀ test. Lactic acid at rest was 48% higher in the blood of group 2 members than in group 1 subjects. No differences were noted in pyruvic acid. The altered lactic to pyruvic acid ratio in the blood of group 2 subjects indicated increased anaerobic glycolysis at very high altitudes. Group 2 also showed a greater buffer deficit, although, blood pH was not significantly altered at rest; there was some elevation of blood glucose.

The graded exercise test induced a 35% higher level of blood lactic acid in group 2 subjects than in group 1. Blood pH was more acid in group 2. In the test of mental work capacity, group 1 subjects had shorter response latencies for visual motor reactions and for selecting a target

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

from two distractors, and higher values of information processing parameters. No differences were found in self-ratings.

Within group 1 the subjects with the highest information processing rate were those in whom the respiratory reaction to moderate hypoxia (in rebreathing) was less pronounced than average. Although the ventilatory response to maximal hypoxia was greater in these subjects, the ceiling of hypoxia endurance was somewhat depressed and blood glucose was higher than average. While the fastest information processors did not differ from the slowest in level of anaerobic glycolysis at rest, in response to exercise, level of lactic acid and ratio of lactic to pyruvic acid was lower in the former than the latter. Physical work capacity was higher for faster information processors, as well. At the higher altitude many of these associations were reversed. The best information processors were characterized by lower reactivity of the respiratory system and greater endurance of maximal hypoxia (higher ceilings), significantly lower blood glucose, more pronounced processes of anaerobic glycolysis at rest and during exercise, and lower physical work capacity. Patterns of correlation between blood sugar and other parameters were very different for the two groups. The authors argue that it is consistent with the data that the metabolism of individuals who at very high altitudes display the lowest psychomotor parameters and highest blood sugars undergoes the greatest transfer to the glutamate shunt with increased synthesis of GABA, which acts as an inhibitory mediator of the CNS. Since GABA enhances the catabolic processes, activates many respiratory enzymes, and improves blood supply to tissues, this metabolic pathway would improve physical work capacity in chronic hypoxia. This would explain the negative association between physical and mental work capacity in temporary residents of very high altitudes.

The author argues that since individual differences have been found to be significant in mental and physical performance during adaptation to chronic hypoxia, they should be considered in selection of individuals for activities involving these conditions.

Table 1: Parameters of higher nervous activity in humans living for 1 year in the mountains

Table 2: Correlations between level of glucose in the blood and other biochemical and physiological parameters

Parameters	Altitude above sea level	
	1680 m	3650 m
Concentration of lactic acid in blood		
before exercise	0.24	-0.44*
after exercise	-0.24	-0.61**
Concentration of pyruvic acid in blood		
before exercise	0.17	-0.33
after exercise	-0.17	-0.43*
Ratio of lactic to pyruvic acid		
before exercise	0.27	-0.48*
after exercise	-0.22	-0.63**
Blood pH		
before exercise	0.17	-0.39*
after exercise	0.44*	0.58**
O ₂ consumption	-0.47*	-0.62**
Endurance to hypoxia	0.32*	-0.62**
Sensitivity to hypoxia	0.51*	-0.31*
Amount of information processed	0.41*	-0.48**
Rate of information processing	0.55*	-0.58**

* correlation significant with $p < 0.05$, ** $p < 0.01$

Figure 1: Parameters of ventilation, gas exchange, sensitivity to hypoxic stimulus, and physical work capacity of humans living at high altitudes for 1 year

Figure 2: Biochemical parameters of blood in humans living at high altitudes for a year at rest and in response to graded physical exercise

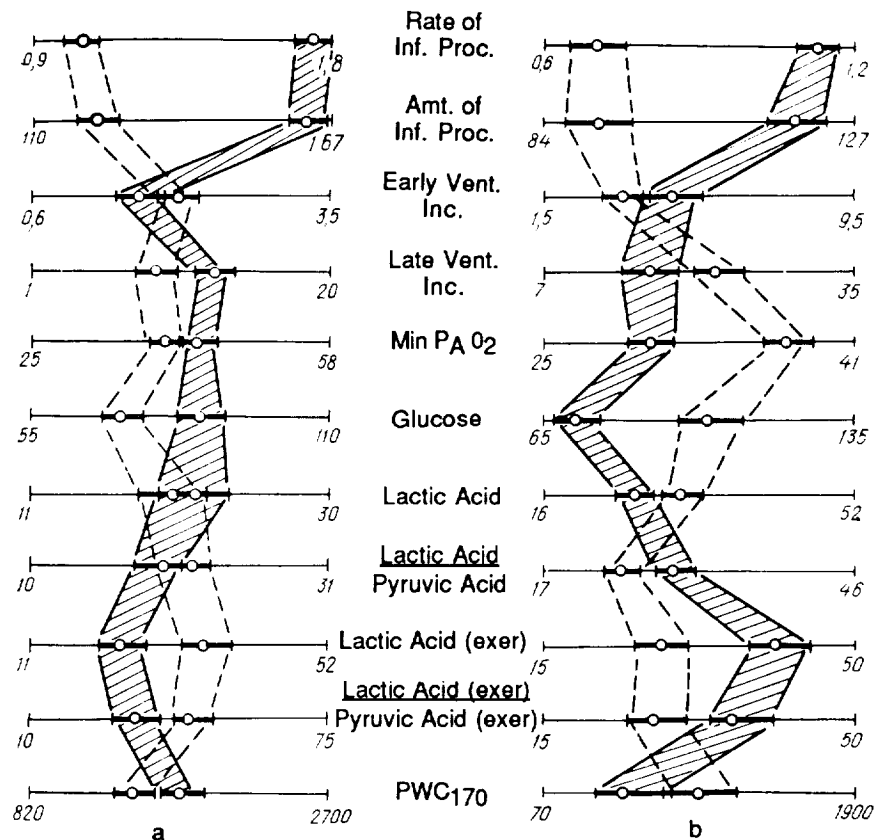


Figure 3: Comparison of characteristics of reactivity of the respiratory system, tolerance of nervous system, carbohydrate metabolism and physical work capacity in subjects with high (hatched area) and low (unhatched area) levels of mental work capacity living for 1 year at altitudes of 1680 m (a) and 3640 m (b)

P1163(25/89) Kolchinskaya AZ, Beloshitskiy PV, Monogarov VD, Pivnutel' RV, Radziyevskiy PA, Krasnyuk AN, Ivashkevich AA, Borisov AN.

Physical work capacity of alpinists under conditions of extremely low pO₂ in inspired air.

Fiziologicheskii Zhurnal.

35(4): 68- 74 ; 1989.

[25 references; 7 in English]

Authors' affiliations: Kiev Institute of Physical Culture

Cardiovascular and Respiratory System, Physical Work Capacity

Humans, Males, Athletes, Alpinists

Hypoxia, Extremely High Altitudes, Exercise

Abstract: Studies were conducted over a 2-year period in hypobaric chambers and on two high mountains in the USSR. Subjects were alpinists in the highest (group 1, n=20) and next highest (group 2, n =26) Soviet qualification category. The following altitudes were studied: altitudes of 2100, 3500, 4200, and 5120 above sea level with pO₂ in inspired air of 130, 103, 92, and 83 mm Hg, respectively; and 4100 and 6100 m above sea level with pO₂ of 92 and 83 mm Hg, respectively ; and 7500 m with pO₂ of 61 mm Hg (barochamber). Each year, 46 athletes were studied of whom 30 participated for 2 years in a row. Work capacity and general condition were evaluated using parameters of work, rate of oxygen consumption, rate of carbon dioxide exhalation, parameters of respiration, blood, rate of mass transfer of oxygen, partial oxygen pressure in alveolar gas, oxygen tension in arterial and mixed venous blood. Changes in oxygen parameters, presence of oxygen debt, changes in parameters of acid-base equilibrium of blood, decrease in blood pH, and increase in concentration of lactate in blood were considered indicators of tissue hypoxia.

At an actual altitude of 2100 m and a hypobaric chamber height of 7500 m the alpinists exercised on a bicycle ergometer with stepped increases in load. Duration of exercise at each stage was 2 minutes, with 2 minutes of rest. Work at the first stages was 1.7, at the second 2.7, at the third 3.7 W/kg body weight. Respiratory parameters and heart rate were recorded during exercise. While subjects were at rest, parameters of central hemodynamics and electrical cardiac activity were recorded. At the remaining altitudes under natural mountain climbing conditions, physical work capacity was estimated using bicycle ergometry and results of time required to climb to a stipulated height. All results were compared to those obtained at sea level during prophylactic examinations of the athletes.

The authors conclude that alpinists retain relatively high work capacity at extremely low pO₂. At pO₂ =61 mm Hg they can do work equivalent to moderate intensity at sea level. At extremely low pO₂, maximal oxygen consumption decreased in qualified alpinists less than work capacity. At pO₂ =61 mm Hg, work capacity decreased by 30.1± 1.4%, and VO₂ max by 17%±7%. Work capacity of alpinists at extremely low pO₂ was limited primarily by decreased muscle tissue capacity to utilize oxygen due to decrease in oxygen pressure in arterial and mixed venous blood below critical levels. Low oxygen pressure in arterial blood led to decreased rate of diffusion of oxygen from blood in the capillaries to cells, decreased oxygen pressure in tissues and decreased rate of oxidative processes. Under conditions of extremely low pO₂, changes occurring in the work capacity of qualified alpinists were subject to individual physiological differences. Work capacity was positively associated with qualification level and duration of participation in the sport, which facilitated high reactivity of respiration in response to pO₂ and efficiency of respiration, and enabled adaptation to low pO₂ in brain, skeletal muscles, and heart tissue.

Table: Parameters of respiration and circulation in qualified alpinists during exercise varying in intensity under conditions of low pO₂

DEVELOPMENTAL BIOLOGY

PAPERS:

P1160(25/89) Serova LV, Denisova LA, Chel'naya NA.

The effect of dynamic factors associated with biosatellite launch and reentry on prenatal development.

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Ontogenez mlekopitayushchikh v nevesomosti . Онтогенез млекопитающих в невесомости [*Ontogeny of mammals in weightlessness.*]

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Developmental Biology, Embryo Experiments, Prenatal Development, Reproductive System
Rats, Fetuses, Pregnant Females

Dynamic Space Flight Factors, Vibration, Linear Acceleration, Impact

Abstract:Embryological experiments on COSMOS biosatellites were preceded by a series of studies evaluating the effects of the vibration, linear acceleration and impact associated with biosatellite launch and reentry, during various stages of prenatal development of Wistar line rats. The prenatal development of mammals is believed to encompass so-called critical periods marked by heightened sensitivity of embryos and fetuses to adverse factors. Recent studies suggest that some factors represent a real danger to the developing organism throughout pregnancy, while others are only risks at particular stages. Data on the effects of the dynamic factors associated with spacecraft launch and reentry — vibration, linear acceleration, and impact on the mother-fetus system, were nonexistent. However, such data were essential for designing flight experiments so as to minimize losses at the launch and reentry stages.

Experiments were performed on 110 pregnant female Wistar rats. Levels of factors were selected to approximate those occurring on COSMOS flights. These levels were:

Vibration — 50-70 Hz, 10 min.

Linear acceleration — 4 g, 10 min.

Impact load — 40-50 g (routine conditions) and 90 g (emergency conditions), 40 msec.

The animals were subjected to the effects of dynamic factors during various stages of pregnancy, beginning with day 3. During exposure they were allowed freedom of movement within the cages used on space flights. In all cases, the state of the reproductive organs and fetuses was evaluated after dissection of the female at the end of pregnancy — on day 21 of fetal development.

Prenatal death rate did not increase after exposure to the combined effects of vibration and linear acceleration (simulation of satellite launch) on days 3, 4, and 8 of pregnancy (each animal was exposed only once). The number of living fetuses in the experimental and control groups was identical. An analogous situation occurred after exposure to impact loads of 40-50 g (touchdown simulation) on days 7, 9, 11, 13, 19, and 21 of pregnancy.

At the same time, after exposure to a combination of vibration and linear acceleration on day 8 of pregnancy and to impact loads on days 7, 9, 11, and 13, the majority of experimental rats displayed placental anomalies never observed in the control (in examination of 1,000 animals). The anomalies took the form of the fusion of one, less frequently two, pair of placentae in each female (Figure 1), accompanied by depressed weight of the fetuses, evidently due to disruption of the nutrient supply. Thus, the effects of dynamic factors associated with biosatellite launch and reentry (vibration, linear acceleration, impact loads) turned out to have an effect on the mother-fetus system, especially during the first half of pregnancy.

The factor that had the most serious consequences in the experiments was impact. When exposure to impact load of 40-50 g (expected level in some instances under routine conditions) occurred on days 7-11 of pregnancy, aside from placental fusion, serious anomalies occurred in fetal development (ectocardia [Figure 2] and umbilical hernia), which were not observed in the control. Exposure to the same level of impact load toward the end of pregnancy (days 19 and 21) did not lead to any serious developmental anomalies in the fetuses.

Exposure to impact levels characteristic of emergency flight situations (approximately 90 g) on days 19 and 21 of pregnancy led to a significant decrease in the number of live neonates and an increased percentage of rats with deviations from the norm, mainly involving bleeding at various sites.

Based on analysis of the material presented above, it was decided to design the first embryological biosatellite experiment so that the rats were exposed to space between days 13 and 20 of pregnancy. This design was tested in a multifactorial ground-based experiment.

Ten female Wistar line rats were exposed to factors associated with biosatellite launch (vibration of 50-70 hz, 10 min.; linear acceleration of 4 g for 10 min.) on day 13 of pregnancy as well as to factors associated with satellite reentry (linear acceleration of 6 g for 10 min.; impact load of about 40 g for 40 msec.) on day 20 of pregnancy.

Parameters of the reproductive function of the female rats, dissected on day 20 of pregnancy 5 hours after exposure to impact, are presented in Table 2. No reliable differences were found between the experimental and control groups in parameters of overall embryonal death rate, number of living fetuses, or weight of fetuses and placentae.

When the fetuses were studied, 27.3% displayed deviations from the norm, mainly in the form of bleeding of variable severity and localization; in the control condition, anomalies were observed in 2.9% of the cases ($p < 0.02$). A tendency was noted for the number of placentae with infarctions and bleeding to increase ($p < 0.05$) in the experimental condition.

Despite the increase in percentage of anomalies, the experimental animals were not retarded in their development compared to control fetuses. As stated above, they did not differ in weight (Table 2), nor did they display differences in hydration or skeletal development. Lengths of ossification sites in various portions of the skeleton were the same for experimental and control groups. These facts suggest that the bleeding occurred directly before dissection as a result of the effects of impact loads. In subsequent development, these impairments are in all probability compensated for by the body, since duration of pregnancy, number of rats in a litter, and their weight at birth were equal in the experimental and control conditions.

The clinical status of the juvenile rats, along with their growth and general development during the first month of postnatal life were also virtually the same for the experimental and control groups. No differences were found in the pattern of weight gain or time to develop an adult coat. The experimental group showed a tendency for the eyes to open earlier, but the difference from the control was not significant.

The results obtained led to the recommendation that embryological biosatellite experiments with mammals involve exposure to space during the last third of pregnancy — the period from 13 to 20 days. Intrauterine exposure to the set of dynamic factors associated with launch and reentry (vibration, linear acceleration, impact) during this period was associated with a litter no different than the control in total number of neonates, physiological maturity at the end of the fetal period and at birth, and rate of development during the first month after birth.

Table 1: Effect of impact loads on the reproductive function of female rats

Group	Number of females				Duration of preg days	Number live in litter	Weight at birth g	Anomalies in %
	1 *	2	3	4				
Control	9	-	-	9	22.0±0.2	10.1±1.2	5.6±0.2	11.1
Day 19	11	0	0	11	22.2±0.1	9.1±1.0	5.8±0.2	11.1
40 g								
Day 19	7	1	3	5	22.6±0.2	4.8±0.8	5.9±0.12	66.7
90 g						p<0.01		p<0.05
Day 21	6	0	2	6	22.3±0.1	8.0±0.7	6.0±0.2	35.7
40 g								
Day 21	6	0	3	5	22.5±0.2	6.0±1.1	5.4±0.4	75.0
90 g						p<0.01		p<0.05

* 1 - initial, 2 - death at impact, 3 - bleeding, 4 - normal birth

Table 2: The effect of the set of factors associated with launch and reentry on the reproductive functions of rats

Group	Total embryo deaths, %	# live fetuses	Weight		Anomalies	
			fetus	placenta	fetus	placenta
Control	23.43±5.60	9.9±0.8	2.4±0.05	0.530±0.2	2.9	5.06
Exper.	13.94±6.05	12.0±0.8	2.59±0.07	0.535±0.2	27.3	12.5
				p<0.01		

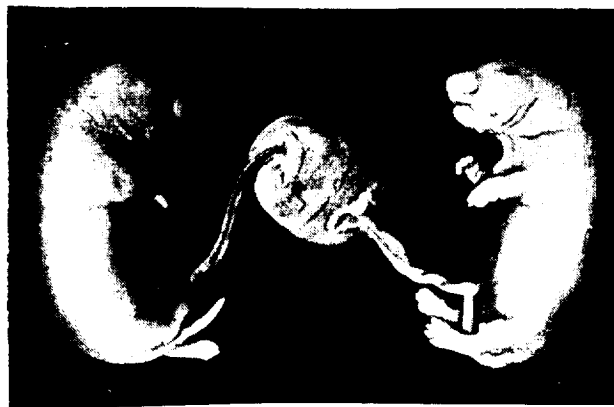


Figure 1: Placental fusion of two adjacent fetuses

Figure 2: Ectocardia of a fetus after exposure to impact on day 7 of prenatal development

P1168(25/89) Serova LV, Denisova LA, Natochin YuV (USSR), Pospishilova I, Pospishil M(Czechoslovakia), Lavrova YeA, Chel'naya NA, Shakhmatova Yel, Meyserov YeS (USSR).

The effect of hypergravity on the development of mammalian fetuses.

In: Gazenko OG (editor).

Ontogenez mlekopitayushchikh v nevesomosti . Ontogenez млекопитающих в невесомости [***Ontogeny of mammals in weightlessness.***]

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Developmental Biology, Prenatal Development, Reproductive System; Musculoskeletal System, Connective Tissue; Hematology, Anemia; Stress Response
Rats, Fetuses, Pregnant Females
Hypergravity, Centrifugation

Abstract: Ground-based simulation experiments were conducted using a centrifuge creating hypergravity of 2-g as a preliminary to the flight of COSMOS-1514.

Previous data show that when the force of gravity changes by ± 1 -g with respect to that of the Earth, along with specific physiological changes, animals undergo general, nonspecific changes, such as retardation of growth, involution of lymphoid organs, lymphopenia, i.e., the classic signs of a stress reaction. These data suggest that the study of the effects of hypergravity of 2-g on the mother-fetus system, aside from being of interest in itself, is a good model for predicting changes that may be expected under conditions of weightlessness.

Ten female rats of the Wistar line (age 5 months) were exposed on a centrifuge from days 14 to 21 of pregnancy. The rate of rotation of the centrifuge was 33.3 rev./min., and its radius was 141 cm. The centrifuge was stopped once a day (from 9:00 to 9:30) for cleaning and feeding of the animals. Reproductive parameters of the experimental animals were compared with parameters of synchronous controls exposed to the factors accompanying centrifugation (noise, motion, air), and also with parameters of pregnant females from a vivarium control group. Animals were examined on day 21 of pregnancy, 5-10 hours after removal from the centrifuge.

During exposure to 2-g from day 14 to 21 of pregnancy, the animals of the experimental group lost weight (3 g), as did animals of the synchronous control, while the norm for those of the vivarium control was a gain of approximately 60 g. The experimental and control groups manifested identical involution of the thymus compared to females of the vivarium control group. No differences were found between the experimental and synchronous conditions in the magnitude of absolute and relative (per 100 g body weight) weight of the kidneys, liver, myocardium, adrenal glands, or spleen.

No differences were found between the animals exposed to centrifugation and those of either control group in concentration of water, sodium, potassium, calcium, copper, and iron in tissues of the myocardium, liver, and tibia bone. In the kidney, especially in the papillary zone, there was a decrease in fluid, iron, and copper and an increase in sodium noted in the animals exposed to hypergravity as well as in those of the synchronous control group. Such changes may be associated with the effects of the non-specific stress factors concomitant with centrifugation.

Pregnancy was accompanied by the development of anemia; in the animals exposed to 2-g, blood hemoglobin decreased and there were significantly fewer erythrocytes in bone marrow than in the vivarium and synchronous control animals. The number of lymphocytes of bone marrow in the experimental group was also significantly lower than in both control groups. The lymphocyte/neutrophil ratio in blood was similarly depressed in all three groups during pregnancy due to decrease in number of lymphocytes and increase in neutrophils (Figure 3).

Investigation of metabolism of nucleic acids in the liver of female rats revealed no differences between the experimental and synchronous controls in RNA and DNA per unit weight, or in activity of RNA-polymerases.

Substantial differences between the experimental and synchronous control groups were found in metabolism of connective tissue. Changes in bone and skin were different in nature (Table 3). In the femur bone of female rats exposed to centrifugation, there was a significant increase in total collagen mainly due to increase of its insoluble fraction. Concentration of soluble collagen changed only slightly; however, the relationship among its subtypes was altered: percentage of type I collagen decreased, while type III, characteristic of growing, active connective tissue, showed a tendency to increase; the percentage of collagen bound with glycoproteins increased. Concentration of glycoproteins in bone also increased; analysis revealed an increase in proportion of fibronectin (an adhesive protein, binding cells and other elements) and a decrease in the proportion of α -glycoprotein. In the skin, changes occurred only in glycoproteins. Although their total concentration was not altered, the proportion of fibronectin was sharply elevated, while the percent of α -glycoprotein was depressed (cf. Table 3).

Summarizing the results of examination of female rats exposed to 2-g, it should be noted that changes of two types were found. Changes of the first type, including growth retardation, involution of the thymus, and others, were observed both in the experimental and the synchronous control conditions and were evidently associated with a general stress response. The second kind of changes were observed only in hypergravity. These included more severe anemia, decreased percentage of lymphocytes in bone marrow, changes in collagen metabolism and in glycoproteins in bone.

No differences were found between the experimental and synchronous control groups in total embryo deaths, or percentage of fetuses and placentae with anomalies (Table 4). The moderate elevation in these parameters in these two groups compared to vivarium animals is evidently due to a stress response in the mother. The numbers of living fetuses in the experimental and control conditions were virtually the same. Morphological characteristics of experimental animals were appropriate to their chronological age.

The weights of fetuses exposed to 2-g were reliably lower than those of the synchronous control (3.71 g and 4.24 g, $p < 0.01$); placenta weight was also depressed in the experimental group. The decreased weight of the fetuses was due mainly to decreased weight of dry substance; concentration of water per kilogram dry tissue was unchanged (Figure 4).

The electrolyte composition of the developing fetuses was studied in detail (Figure 4). Despite their decreased body weight, the total concentrations of potassium, calcium, magnesium, copper, and iron in the fetuses developing in hypergravity were not depressed. For this reason when they were calculated per unit tissue, and especially dry tissue, the concentrations of potassium, calcium, and iron were higher than in the fetuses of the synchronous groups. Despite the fact that the total concentration of calcium in the fetuses of animals exposed to centrifugation was unaltered, they displayed retardation in skeletal development, evidently associated with delay in incorporation of calcium in bone. The delayed development of the skeleton in fetuses of the experimental group took the form of a reliable decrease in the dimensions of ossification sites in the bones of the fore and hind legs, decreased bone length, and increased width of the fontanel compared to fetuses in the synchronous and vivarium control groups (Tables 4, 5).

A comparative investigation of liver metabolism in fetuses of the experimental and synchronous control groups revealed no differences in concentrations of RNA, DNA, or in activity of RNA polymerases.

Thus, exposure of female rats to 2-g in the last third of pregnancy did not prevent the development of a normal number of living fetuses, in spite of the stress response in the mother's body, accompanied by significant activation of catabolic processes and growth retardation. Deviation of the state of experimental fetuses from the control were slight, amounting to a slight delay in growth and development of the skeleton.

These results are encouraging with respect to the possibility that mammal fetuses could survive prenatal exposure to weightlessness during the last third of pregnancy. The results of the embryological experiment on COSMOS 1514 confirmed this hypothesis.

Table 3: Metabolism of connective tissue in rats, exposed to 2-g on days 14-21 of pregnancy

Grp	n	Total mg	Pepsin soluble %	Collagen Type I %	Type III %	Glyco- protein mg	Fibro- nectin %	Acid a- glycoprot. %
Femur Bone								
Exp	10	43.0±4.2	648.1±20.4	37.0±3.4	30.0±3.4	1.31±0.05	74.0±0.8	26.0±0.8
		p<0.01		p<0.05		p<0.05	p<0.01	p<0.01
Sync.	5	26.1±3.5	596.0±13.2	62.0±1.8	22.0±2.5	0.70±0.04	67.0±0.9	33.0±0.6
Skin								
Exp.	10	7.9±1.9	565.0±11.8	44.0±1.2	27.0±1.9		0.28*81.0±1.0	19.0±1.1
							p<0.01	p<0.01
	5	8.8±2.2	558.0±9.4	46.0±0.5	23.0±2.3	0.24	26.0±10.9	74.0±10.9

* For technical reasons these are the results of a single combined sample

Table 4: Parameters of reproductive functions of female rats exposed to 2g from days 14 to 21 of pregnancy

Group	n	Corpora lutea, n	Implantation sites, n	Resorptions, n	Embryo Live deaths, n	fetuses	Anomalies, fetuses placent
Exp.	10	14.8±0.7	10.8±1.6	1.2±0.4	24.2±4.2	10.1±0.6	8 7
					p _v <0.05		
SC	5	13.5±0.7	11.3±0.8	1.2±0.4	35.0±10.8	9.6±1.6	8 6.3
VC	15	14.4±0.8	13.2±0.7	0.6±0.2	12.6±2.6	11.4±0.6	0 1.6

Table 5: Development of the skeleton in the fetuses of rats exposed to 2g from days 14 to 21 of pregnancy

Group	n	Femur	Tibia	Length of ossification Iliac	Ulnar	sites, mm Scapular	Width of fontanel, mm
Exp.	17	2.4±0.05	3.0±0.05	2.0±0.03	3.5±0.04	3.0±0.04	2.9±0.05
		p _v ,s<0.01	p _v <0.002	p _v <0.01	p _v <0.001	p _v <0.02	p _v ,s<0.002
				p _s <0.02	p _s <0.02		
SC	10	2.6±0.05	3.2±0.1	2.1±0.02	3.8±0.1	3.1±0.05	2.5±0.1
						p _v <0.02	
VC	10	2.6±0.04	3.4±0.1	2.2±0.05	4.0±0.1	3.4±0.1	2.5±0.1

On days 217-219 of flight, concentrations of catecholamines in blood exceeded baseline in all three cosmonauts participating in the 237-day flight. After reentry the level of noradrenalin decreased in blood, but did not return to baseline, increasing again in two subjects on day 8. Postflight plasma adrenalin exceeded baseline, but remained within normal limits. On days 217-219 of flight, excretion of adrenalin and noradrenalin were at preflight levels in two of the three subjects. Excretion of metanephrine, normetanephrine, dopamine, vanillylmandelic acid, and homovanillic acid was depressed compared to preflight level. Postflight, excretion of all catecholamines, their metabolites, and DOPA increased above preflight values. Activation of the hormonal component of the sympathetic adrenal system (A/NA) was elevated during the readaptation period in all subjects, but varied in extent, while relative activity of adrenalin methylation was depressed. Adrenalin conjugation was depressed. These changes point to activation of the hormonal component postflight. Relative activity of noradrenalin synthesis (NA/DA) was elevated compared to preflight in two of the three cosmonauts. Relative activation of noradrenalin methylation (NMN/NA) was below baseline in all subjects. Relative activity of dopamine synthesis (DA/D) was higher in one cosmonaut and lower in the other two, with elevated dopamine inactivation. Relative activity of catecholamine deamination was at baseline level in two subjects and elevated in one. Overall level of secretion was above baseline in all cosmonauts.

The authors argue that the low level of changes in parameters of the sympathetic adrenal system during the 237-day flight suggest good adaptation to weightlessness and other space flight factors. Decreased excretion of metanephrine and normetanephrine with catecholamine excretion unaltered, is interpreted as a result of decreased methylation to support normal levels of catecholamine circulation and normal sympathetic adrenal system activity on long-term space flights. An analogous mechanism is hypothesized to operate for dopamine metabolism. Lack of decrease in the mediator component of the sympathetic adrenal system, as occurs during weightlessness simulation, is attributed to success of the inflight physical conditioning program. During reentry, the level of catecholamines in blood remained at preflight level while their renal excretion decreased. These results, suggesting decreased sympathetic adrenal system activity during the transition from weightlessness to gravity, require further study.

The activation of the sympathetic adrenal system observed after long-term flights, reached a maximum on days 3-8 of recovery. The mediator component of the system was particularly affected and concurrent changes in noradrenalin and dopamine served to support the elevated level. Increased DOPA excretion postflight suggests a high reserve potential for the sympathetic adrenal system, a characteristic of highly trained individuals.

ENDOCRINOLOGY

Table 1: Renal excretion of catecholamine and its metabolites in a cosmonaut (1) completing a 211-day flight

Parameter	Norm	Pre-flight	0	* *	+ 1	+ 2	+ 3	Postflight				
								+ 4	+ 5	+ 6	+ 7	+ 8
A, µg/day												
Free	5-15.0	16.0	25.0	38.0	40.0	39.6	37.8	39.0	34.3	28.5	20.1	
Bound	Up to 40	31.6	38.0	55.3	62.5	66.0	57.2	52.3	48.7	45.0	40.0	
Na, µg/day												
Free	20-40	32.0	20.0	41.0	53.0	66.5	60.8	59.0	54.7	47.3	44.2	
Bound	Up to 50	35.7	30.0	45.7	48.3	52.0	56.0	51.0	57.2	54.0	50.3	
DA, µg/day												
Free	112-450	281.0	386.0	447.0	473.0	469.0	457.0	437.0	407.0	392.0	387.0	
Bound	Up to 500	443.0	360.0	420.0	507.0	529.0	543.0	552.0	530.0	518.0	501.0	
DOPA, µg/day	8-111	32.0	18.3	28.3	42.5	66.0	74.0	70.2	61.3	57.3	50.2	
MN, µg/day												
Free	130-180	160.0	118.0	171.0	197.0	218.0	207.0	192.0	185.0	174.0	172.0	
Bound	100-160	133.0	93.0	140.0	156.0	160.0	159.0	154.0	153.0	147.0	130.0	
NMN, µg/day												
Free	90-140	125.0	70.3	97.0	128.0	154.0	179.0	193.0	188.0	80.0*	169.0	
Bound	60-100	87.0	48.0	46.0	53.0	60.0	68.0	72.0	70.1	84.0	95.0	
VMA, mg/day	1.9-6.3	3.25	3.90	5.10	6.09	7.20	6.88	8.20	8.10	7.80	6.30	
HVA, mg/day	1.6-3.5	2.40	4.20	4.60	5.20	6.00	6.20	8.30	5.80	5.46	4.48	

* sic; **0 is the day of reentry

Table 2: Renal excretion of catecholamine and its metabolites in a cosmonaut (2) completing a 211-day flight

Parameter	Norm	Pre-flight	0	+1	+ 2	Postflight				
						+3	+4	+5	+ 6	+ 4 5
A, µg/day										
Free	5-15.0	15.1	19.0	28.3	32.9	29.0	26.4	23.5	18.6	13.2
Bound	Up to 40	31.0	28.5	49.0	57.4	60.8	56.0	46.3	42.5	—
Na, µg/day										
Free	20-40	30.2	16.8	38.5	58.0	63.7	72.0	70.5	64.0	38.3
Bound	Up to 50	36.8	28.5	36.8	50.5	57.3	68.0	67.3	60.5	—
DA, µg/day										
Free	112-450	269.0	400.0	460.0	471.0	465.0	453.0	439.0	399.0	370.0
Bound	Up to 500	470.0	375.0	397.0	460.0	510.0	538.0	540.0	536.0	—
DOPA, µg/day	8-111	32.7	20.6	32.8	47.6	56.3	68.0	70.2	63.0	36.1
MN, µg/day										
Free	130-180	157.0	121.0	167.0	180.0	196.0	200.0	199.0	190.5	153.0
Bound	100-160	131.0	100.0	137.0	145.0	151.0	157.0	149.0	141.0	—
NMN, µg/day										
Free	90-140	126.5	67.0	110.0	144.0	162.0	168.0	178.0	165.0	140.0
Bound	60-100	104.0	54.0	57.0	60.0	71.0	78.0	97.0	119.0	—
VMA, mg/day	1.9-6.3	3.00	5.60	6.71	7.80	8.36	8.58	7.60	6.50	3.50
HVA, mg/day	1.6-3.5	1.98	3.20	4.70	6.20	7.78	7.90	6.90	5.80	2.84

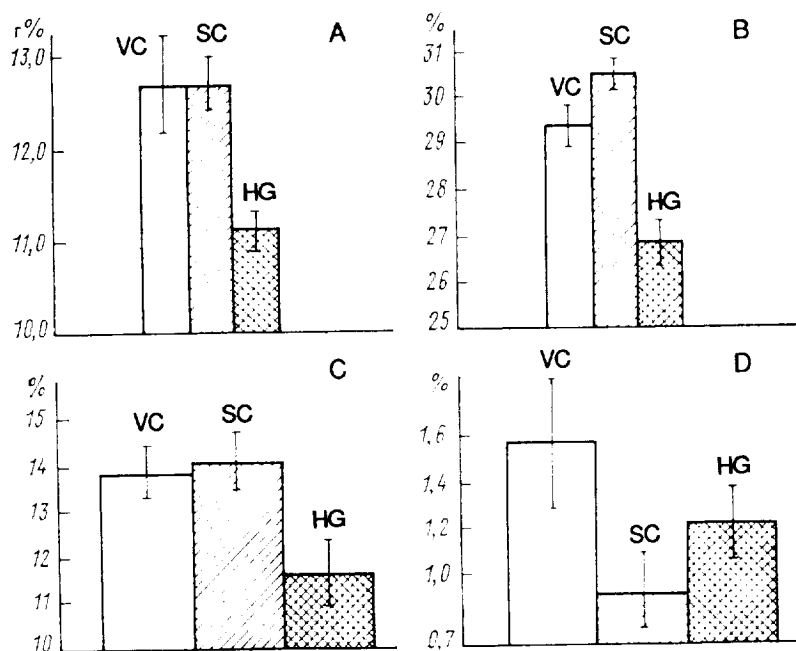


Figure 3: Certain hematological characteristics of female rats exposed to 2g during pregnancy; blood hemoglobin (A); cells of the erythroblast cambium (B) and lymphocytes (C) of bone marrow lymphocyte/neutrophil ratio in blood (D)

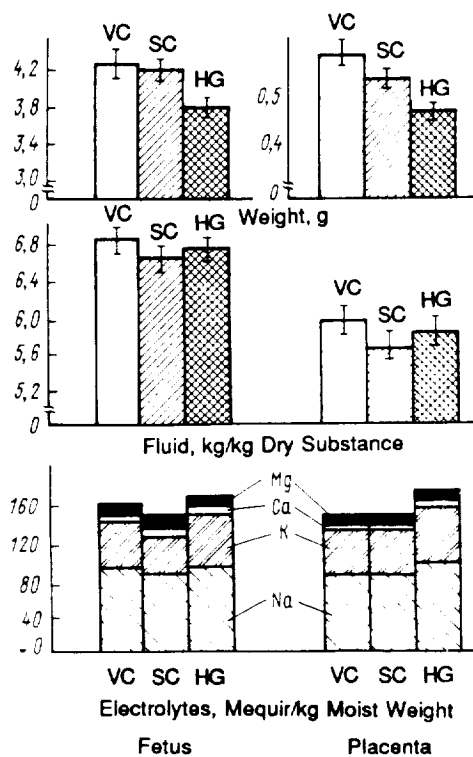


Figure 4: The effects of hypergravity of magnitude 2-g on weight of fetuses and placentae, their water and electrolyte contents

ENDOCRINOLOGY

PAPER:

P1129(25/89)* Davydova NA, Kvetnyanski R, Ushakov AS (USSR, Czechoslovakia). *Sympathetic-adrenal responses of cosmonauts after long-term space flights on Salyut-7.*

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 14-20; 1989.

[21 references; 14 in English]

Endocrinology, Sympathetic Adrenal Responses

Humans, Cosmonauts

Space Flight, Long-Term, Salyut-7

Abstract: The work was directed at investigating parameters of catecholamine metabolism in the blood plasma and daily urine of cosmonauts during and after flights of 211 and 237 days. Samples were taken from the two cosmonauts completing the 211-day flight on 30 days preflight, during the first 8 days of flight, and on day 45 of readaptation. For the 237 day flight, blood was taken from the 3 cosmonauts 30 days preflight, inflight and on days 1 and 8 of readaptation; and urine was collected 30 days preflight, inflight, and on days 3-5 of readaptation. Blood was taken from these cosmonauts on days 217-19 of flight with the Plasma-01 instrument, which was used to take venous blood, centrifuge it, separate plasma from erythrocytes and freeze it at -30°C. Plasma as well as daily urine was stored in a frozen state on the station and then returned to Earth for analysis. Radioenzymatic methods were used to determine plasma adrenalin, and noradrenalin concentrations, as well as adrenalin, noradrenalin and dopamine in urine. Renal excretion of free and bound adrenalin, noradrenalin, DOPA, metanephrine, and normetanephrine was measured fluorometrically, while excretion of vanillylmandelic and homovanillic acids was measured using thin-layer chromatography. Comparison of results obtained using the radioenzymatic and fluorometric methods revealed no qualitative differences. Ratios were computed between the different catecholamines and their metabolites, as an additional technique for assessing activity of the sympathetic-adrenal system.

Preflight parameters for all subjects were within the norm. On the day of reentry after the 211-day flight, cosmonauts' excretion of adrenalin, vanillylmandelic acid and homovanillic acid was above baseline, while excretion of noradrenalin, dopamine, DOPA, metanephrine, and normetanephrine was below preflight values. Subsequently, excretion of catecholamine and DOPA metabolites gradually increased, exceeding preflight values by days 3-6 of readaptation. Normalization had not occurred on day 8, but on day 45 all parameters were normal. The ratio of adrenalin to noradrenalin was twice baseline in both subjects on the day of reentry and then decreased. The ratio of metanephrine to adrenalin (indicator of methylation of adrenalin) was elevated during readaptation in one cosmonaut and depressed in the other. The noradrenalin : dopamine ration was depressed initially after reentry and then increased, remaining within normal limits. The dopamine : DOPA ratio changed in the opposite direction to the above. The relative activity of methylation of noradrenaline (NMA:NA) was depressed, while processes of dopamine inactivation (HVA:DA) were elevated. The relative activity of the process of catecholamine deactivation exceeded preflight values. Overall level of secretion of all substances studied exceeded the preflight level.

The authors conclude that after this flight the hormonal component of the sympathetic adrenal system was activated on the day of reentry, while the mediator component was depressed; however, during readaptation the mediator component was activated with changes in the metabolic processes in the system.

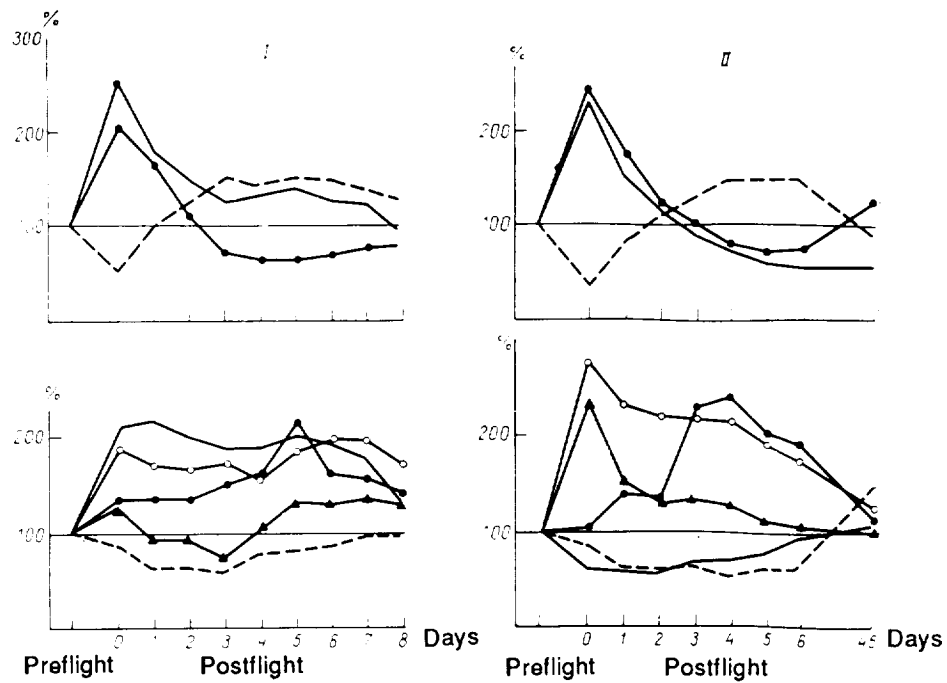


Figure 1: Parameters of relative metabolic activity of catecholamines and their metabolites in cosmonaut No. 1 (I) and No. 2 (II), after completion of a 211-day space flight (preflight level is taken as 100%)

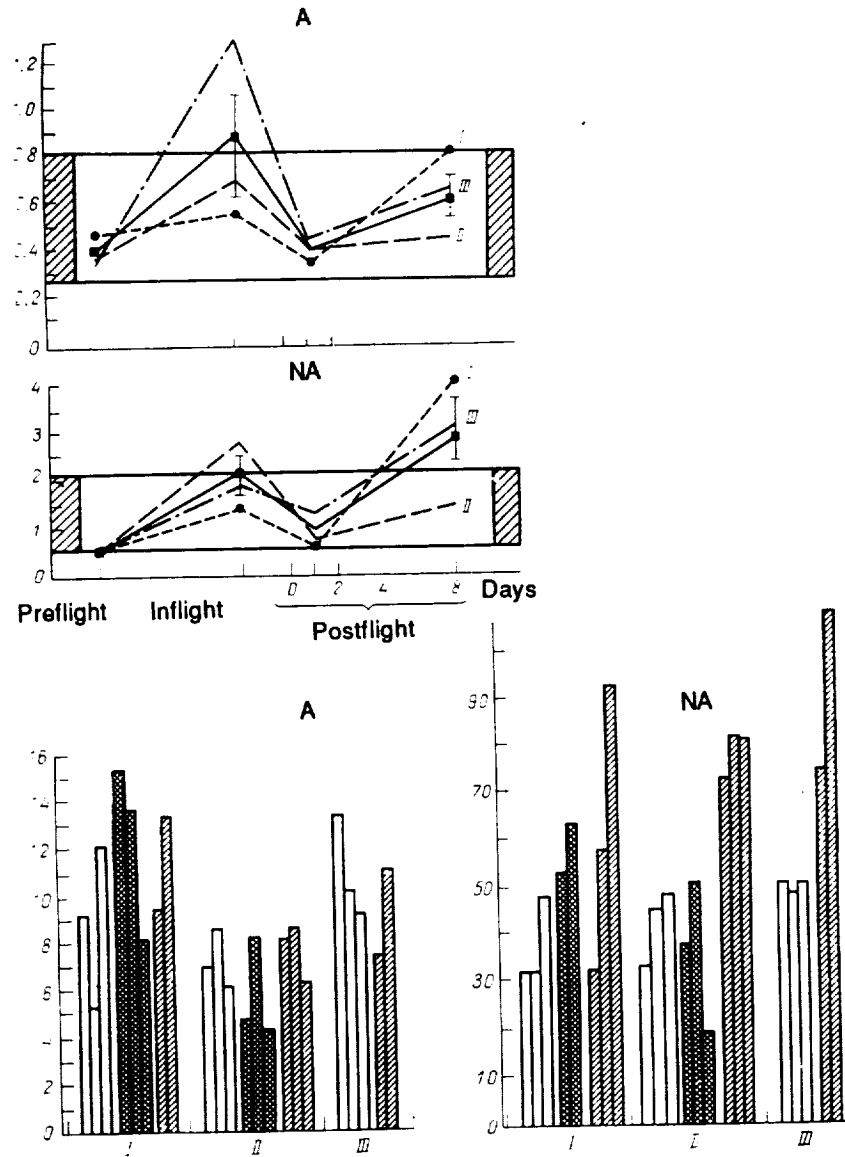


Figure 2: Concentration of (a) adrenalin and noradrenalin (in pmoles ml⁻¹) in the blood of three cosmonauts sampled on board the space station during a 237-day flight and renal excretion (b) A (in μg/day) and NA (μg/day) in these same cosmonauts. Here and in Figure 3, I, II, and III indicate three cosmonauts; light columns - preflight; filled columns - inflight; hatched columns - postflight

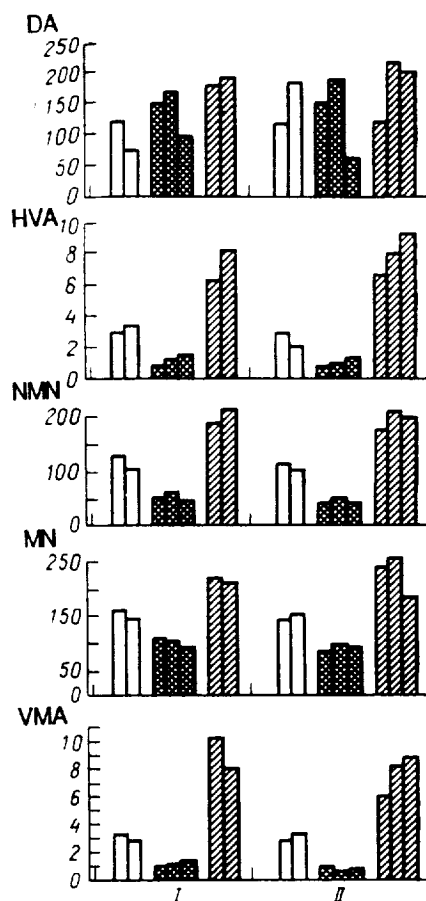


Figure 3: Renal excretion of dopamine (in $\mu\text{g/day}$), homovanillic acid (in mg/day), normetanephrine (in $\mu\text{g/day}$), metanephrine (in $\mu\text{g/day}$), and vanillylmandelic acid (in mg/day) in cosmonauts completing a 237-day flight

EQUIPMENT AND INSTRUMENTATION

PAPERS:

P1144(25/89)* Barer AS, Konakhevich YuG, Sholpo LN, Kurme DA, Leytene LYa.
Differential criteria for head impact tolerance in approving protective devices.
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.
23(4): 76-79; 1989.
[7 references; none in English]

Equipment and Instrumentation, Head Protection, Safety Criteria
Humans
Impact

Abstract: When devices to protect the head from impacts are evaluated and approved in aviation, criteria pertain to retention of the capacity of a pilot or other crewmember to save himself in the emergency situation. However, the authors argue that in some situations the individual's capacity to save himself after impact is not that crucial, in which case the above criterion may be too rigid. They propose a more flexible set of criteria for protective devices that account for the possibility that other people may be available to save the pilot. Development of these more flexible criteria had three stages: selection of clinical parameters for differential evaluation of the consequences of a blow to the head; establishment of the function relating clinical manifestations of craniocerebral trauma to the parameters of the impact and its localization; and selection of critical parameters for impact blows to the head for differential evaluation of protective devices during the approval process. Three factors were identified: A - loss of consciousness and its duration; B - impairment of general state and the requirement for immediate medical care; and C - the possibility of professional rehabilitation. The latter two factors could be assigned a number ranging from 0 (absence of adverse consequences) to 2.00 (unacceptable level of the factor). Factor A ranged from 0 to 4. A coefficient D was defined as equal to 1/4 of the sum of the values of factors A, B, and C. A total D value less than or equal to 1 would typically be considered acceptable. This value would not always include the criterion that the pilot could save himself without outside help. This criterion could be dispensed with in situations where immediate medical help is available. On the basis of type of accident the protective device is designed for, particular D values involving only some subset of the three factors may be used in evaluating a device.

Table 1: Ranked value of factors for evaluating the consequences of a blow to the head

Table 2: Ranked value of factor D

Table 3: Ranked value of parameters of D for maximal values of factors A, B, and C

Figure: Curves for predicting consequences of a blow to the head as a function of maximal contact force and location of blow

P1147(25/89)* Simonov LG, Alekberov MI.

Ultrasound devices for continuous investigations of nonelectric processes in the human skull.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 86-88; 1989.

[10 references; 1 in English]

Equipment and Instrumentation, Ultrasound

Humans

Skull, Nonelectrical Processes

Abstract: This paper describes a device for manual guidance of an ultrasound beam to be used for investigating intracranial processes. This device consists of a cylindrical case with a radius of curvature corresponding to the surface of a piezotransformer holder. The case is filled with acoustically transparent fluid, and covered with an elastic oil-resistant membrane. The case contains six springloaded ball bearings fitted with adjustment screws, which allow the position of the piezotransformer to be adjusted with minimal friction, and to be secured when the desired position is found. This device allows the angle of input of ultrasound to be changed by up to 15°. The device was tested experimentally and was found to support long-term ultrasound recording of nonelectric fluctuations within the skull.

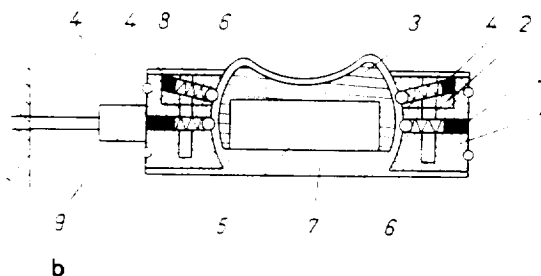


Figure 1: A device for manual guidance of an ultrasound beam

a - URN-03; b - diagram of a cross-section of URN-03; 1 - outer case; 2 - inner case; 3 - piezotransformer holder; 4 - spring-loaded ball bearings with adjustment screws; 5 - piezotransformer; 6 - elastic membrane; 7 - acoustically transparent fluid; 8 - reinforcing screws; 9 - plug with outlet lead

Figure 2: Diagram of electronic guidance

EXO BIOLOGY

PAPER:

P1153(25/89) Kustov VV, Belkin VI, Kruglikov GG.

On the mechanisms underlying the biological effects of lunar soil.

In:) Malkin VB, Kosmolinskiy FP, Kuznets Yel (editors).

Chelovek i Kosmos: Idei K.E. Tsiolkovskogo i ikh razvitiye v sovremennoy biomeditsine. Trudy XXII Chteniy, posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idej K.E.

Tsiolkovskogo (Kaluga, 15-18 sentyabrya 1987) Человек и Космос Идеи К.Э. Циолковского и их Развитие в современной биомедицине. Труды XXII Чтений; посвященных разработке научного наследия и развитию идей К.Э. Циолковского (Калуга; 15-18 сентября 1987)

Man and space: The Ideas of K.E. Tsiolkovskiy and their development in modern biomedicine. Works from the XXII lecture series devoted to development of the scientific

heritage and development of the ideas of K.E. Tsiolkovskiy (Kaluga, 15-18 September, 1987) Moscow: Soviet Academy of Sciences; 1988.

Pages 48-53

[20 references; 5 in English]

Exobiology, Biological Effects

Mice

Lunar Soil, Superparamagnetism

Abstract: Experiments were performed on outbred male mice weighing 22-24 g. The animals were divided into four groups. In animals of all groups sterilized porolon capsules were affixed under the skin of the shoulder. In group 1, this capsules contained particles of agglomerates from the Mare basins of the lunar surface; in group 2 the capsules contained grains of plagioclase, olivines, and orthopyroxenes from the subsoil region of the Moon; group 3's capsules held particles of terrestrial plagioclase; while the capsules for group 4 were empty. Particle size varied between 0.5 and 1.0 mm, and weight ranged from 0.11 to 0.87 mg. Agglomerates from the lunar maria were dark aggregates of complex branching form, consisting of agglomerated grains of fine fractions of lunar substance. A characteristic trait of the agglomerates was their high concentration of finely dispersed forms of superparamagnetic iron. These forms of iron were also present, but in smaller quantities, on the surface particles and grains of minerals from the subsoil region of the Moon. Terrestrial particles were identical in their size and mineral composition to the corresponding lunar particles, but did not contain any finely dispersed superparamagnetic iron. This unique property of lunar soil allowed its reactive activity to be assessed using the method of paramagnetic resonance. On days 14, 42, 61, 81, 105 and 120 after capsules were implanted, some mice in each group were sacrificed and the particles removed from the subjects and weighted. Spectra of electromagnetic resonance were recorded on radiospectrometers in the z-range at a temperature of 25° C. These capsules were then affixed under the skin of another group of subjects. The biological effects of the particles were assessed on the basis of their effect on the general state and behavior of the animals, and on the state of cellular reactions in the area of the capsule. Cytological composition and structural functional state of the cells were examined using a light microscope, along with the number of macrophages and giant multi- and binucleate cells with and without phagocytosed particles of cellular detritus in the cytoplasm, and also the number of lymphocytes, neutrophils, eosinophils, fibroblasts, and destructive cells in the exudate. Results were expressed in percentages.

It was found that the histological medium significantly altered the reactive activity of the lunar soil particles. When implanted in animals the concentration of finely dispersed forms of superparamagnetic iron decreased (disappearing in some cases), especially on the surface of the particles, in particles directly in contact with tissue, but remained virtually unaltered in agglomerates that did not disintegrate.

Lunar particles had no effects on the general state or behavior of the animals. Smears from exudates of animals exposed to lunar soil showed greater numbers of neutrophils, phagocytosed and nonphagocytosed macrophages, and also giant multinucleated cells. The increase was most pronounced when agglomerates were implanted. After 14- to 28-day contact there was a significant quantity of eosinophils in the exudate of wounds containing all the particles studied. These cells were virtually absent in the exudates of the control experiments. During the subsequent 15 to 20 days, the quantity of eosinophils increased only in exudates with implantation of agglomerate.

Concentration of disintegrating (dying) cells in exudate increased after contact with lunar substance. Such cells constituted 52, 40, 12, and 10%, in groups 1-4, respectively. During the subsequent 20- and 28- day contacts, contact between agglomerates and the biological medium increased the concentration of such cells to 31-25% [sic.]. The authors conclude that particles of lunar soil are not biologically inert; the extent of their biological activity depends on the level of reactive activity of the particles on their surface.

HABITABILITY AND ENVIRONMENT EFFECTS

P1148(25/89)* Surovezhin IN.

Group gas-chromatographic identification of limit values of alcohols in hygienic studies.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 89-90; 1989.

[5 references; 2 in English]

Habitability and Environment Effects, Hygienic Studies, Toxicology

Alcohols, Limit Values

Equipment and Instrumentation, Gas Chromatography, Group

Abstract: The technique used in toxicological analysis of gases in an environment involves gas chromatographic identification of individual gases by matching parameters with a calibrated table. However, sometimes exact matches cannot be found in the table because toxicological properties have not been established, and evaluation proceeds by analogy. Frequently, once the class and group of the gas is determined, identification of the individual substance adds nothing further to the toxicological evaluation. The author has developed a technique for group identification of limit values of alcohols. Local indexes were calculated on the basis of retention indexes for columns with Apiezon L polyphenyl alcohol, QF-1 and PEG? 20 m. Parameters of isomerization and the difference between local indexes were obtained in columns of various polarity. Toxicological parameters were taken from a handbook.

The authors argue that their data show that the toxicity of branching? primary alcohols cannot be less than for linear primary alcohols, but may be close to the toxicity of secondary linear alcohols. Secondary branching alcohols probably occupy an intermediate position between secondary linear and tertiary alcohols. The authors conclude that their method makes it possible to evaluate toxicity of limit values of alcohols without individual identification, or can precede individual identification. The method of group gas chromatographic identification can also be applied to chemical analysis of aldehydes, ketones, and complex esters.

HUMAN PERFORMANCE

P1132(25/89)* Oboznov AA, Ponomarenko VA, Arkhangel'skiy DYu.

Psychological preparation of operators for performance under conditions of prolonged acceleration.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 26-29; 1989.

[3 references; none in English]

Human Performance, Operator Performance, Tracking

Humans, Operators

Psychology, Pretraining, Acceleration, Prolonged

Abstract: This experiment was conducted in two stages. In the first, performed under normal conditions, subjects acquired the skill of two-dimensional compensatory tracking of a target moving along a trajectory on a CRT. The set-up contained an adaptive circuit that changed the brightness of the target when the operator tensed the leg and stomach muscles in the way recommended for protection against the effects of acceleration. To maintain target brightness the subject had to keep these muscles tensed throughout task performance. The total of eight subjects was divided into two groups of four. One group used the adaptive circuit, the other did not. The second stage of the experiment was conducted on a centrifuge creating a $+G_z$ force of 5 units with an increase gradient of 1-g/second. In preliminary rotations, operators of both groups were taught the protective movements during acceleration without performing the tracking task. Then all subjects participated in 7-8 rotations (over the course of 1 month), during which they performed the tracking task. The task was run for 60 seconds, and performance parameters were recorded by computer. A tracking error parameter was used as a measure of performance. Subjects responded to a questionnaire about their concentration.

In the first experiment, it was determined that the operators required to maintain muscle tension while performing the tracking task, performed no worse than other subjects. In the former group, attention was directed primarily at the tracking task. Under exposure to acceleration, tracking performance of the group that had previously combined task performance and muscle tension was 1.4 times better than that of the control group, which had never combined the two requirements. Questionnaire responses suggested that control subjects directed primary attention to maintaining muscle tension, to the decrement of task performance. Toward the end of the experiment, however, the control group had mastered the skill of combining both tasks; their tracking performance was no worse than that of the pretrained group.

Table: Tracking accuracy and attention allocation in operators of the experimental and control groups

Figure: Tracking error in the first two and last two rotations on the centrifuge

P1146(25/89)* Yablonko YuP, Anishchenko VF.

Analysis of techniques for displaying information to operators performing control tasks.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 83-85; 1989.

[20 references; 9 in English]

Human Performance, Control Tasks

Humans, Operators

Man-Machine Systems, Information Displays; Mathematical Modeling

Abstract: This paper models an analog and a digital mode of displaying information to an operator engaged in control of a moving object. The information processing approach adopted is based on consideration of the changes in entropy of the controlled object. The rate of change in entropy characterizes the information flow which the operator must deal with during task performance. The experimental part of the study involved determination of the time required to move the controlled object from the initial to the final state. For each display device, 150 runs were performed. These data were used to derive a measure of information load on the operator through formulae included in the model.

Figure 1: Structure of the control contour

Figure 2: Functions of density and probability of magnitude of information flow for digital and analog information representations

Figure 3: Distribution of probable magnitudes of information flows for control using analog and digital displays

IMMUNOLOGY

PAPERS:

P1170(25/89) Konstantinova IV.

Prospects for the study of changes in the immune system that mediate disruptions of calcium metabolism in bone tissues under conditions of weightlessness and hypokinesia.

In: Konstantinova IV.

Sistema Immuniteta v Ekstremal'nykh Usloviyakh: Kosmicheskaya Immunologiya. Система Иммуитета в Экстремальных Условиях: Космическая Иммунология [***The Immune System Under Extreme Conditions: Space Immunology***] No. 59 in the series Problemy Kosmicheskoy Biologii. Проблемы Космической Биологии. [Problems of Space Biology]. Moscow: Nauka; 1988.

Pages 191-209.

Immunology, Musculoskeletal System, Bones, Metabolism, Calcium Metabolism;
Osteoclast Activating Factor
Humans, Cosmonauts; Rats; Mice
Space Flight, Weightlessness

Abstract: Alteration of calcium metabolism in response to long-term exposure to weightlessness is one of the most universally acknowledged and well-documented phenomena of space medicine. During space flight, bone tissues lose minerals, especially calcium. American Gemini and Skylab data showed that in space, catabolism predominates in bone tissue, leading to negative calcium and phosphorus balance and decreased mineralization. The loss rate amounts to approximately 200 mg Ca per day or 6 g per month. Soviet space researchers established that during long-term flights there is a relative increase in renal excretion of osmotically active substances, particularly potassium and calcium. In flights lasting from 30 to 175 days the highest levels of renal excretion of electrolytes occur toward the end of the first month.

When effects of weightlessness are simulated during long-term hypokinesia, changes in calcium-phosphorus metabolism and bone demineralization have been demonstrated. In addition, animals exposed to long-term hypokinesia have demonstrated inhibition of enchondral and periosteal osteogenesis, osteoporosis of spongy bone, and perilacunary osteolysis of compact bone.

In studies of formation of bone tissue in adult and developing rats exposed to space on COSMOS biosatellites, it was demonstrated that the growth rate of cortical and trabecular bone is diminished, as is bone strength. Periosteal growth is retarded, while endosteal growth rate remains normal. Some investigators failed to find any effects of flight on bone tissue resorption. Others, using other methods, demonstrated moderate activation of resorption in flight rats. It is not clear to what extent these results can be extrapolated to humans. French researchers have found that long-duration immobilization of humans leads to marked activation of osteoclasts, leading in turn to bone resorption, while osteoblast activity decreases.

There is a great deal of evidence linking the immune system with the regulatory processes controlling the mineral saturation, growth and remodeling of bone tissue. Some immune system disorders (runt disease) are associated with termination of bone growth.

Researchers interested in bone calcification disorders focus on two types of cells — osteoblasts and osteoclasts. Osteoblasts differentiate from mesenchymal cells and then from circulating stem cells of bone marrow. Osteoclasts, in some views, form as a result of merging of

precursors of mononuclear cells, although other data suggest that they come from a separate cellular line of the monocyte series. Another possibility is that they arise from hemopoietic stem cells. Considerable data suggests that there is a close linkage between the regulation of calcium metabolism in bone tissue and osteoclast functioning on one hand and thymus and bone marrow functioning on the other. Heritable osteoporosis (based on a resorption defect) serves as a good model for study of mineral saturation in bones and its association with the immune system. Mice with this hereditary defect can be restored to normal by injection of spleen and bone marrow cells from normal rats; and normal rats will develop osteoporosis after receipt of analogous cells from osteoporotic mutants. Similar effects were achieved through parabiosis. These results suggest that control of the bone modeling and remodeling processes is effected by migrating cell of the myelin series. Rodents with osteoporosis also show certain immune defects: decreased proliferative response to T- and B-mitogens, deficits in macrophages, delay in transplant rejection, thymus atrophy. Many bone problems in animals with these defects can be cured, temporarily at least, by injection of thymus, lymphoid, or bone marrow cells. Diphosphonates, which interfere with calcium metabolism, when injected for 30 days into rats, create osteoporosis, and also a number of changes in the immune system typical of runt disease, including sharp decrease in thymus size.

The processes of resorption and formation of bone tissue are regulated by many humoral factors. Some of these seem to play a leading role in local bone remodeling, and others regulate calcium metabolism. These factors include lymphokines, monokines, and also complement. Of particular interest is the osteoclast-activating factor (OAF), which was first isolated in the study of gum disease. OAF is produced by leukocytes of peripheral blood of healthy donors, activated by PHA and other mitogens, as well as by lymphocytes in the presence of the antigen to which they are sensitive.

The effects of OAF on bone tissue *in vitro* are in many respects analogous to the effects of parathyroid hormone: both lead to long-duration resorption of embryonal tubular bones; both inhibit collagen synthesis from embryonal calvaria, and both block calcitonin and phosphate. They differ in their sensitivity to glucocorticoids.

Study of the process of bone tissue resorption in various chronic inflammatory processes and neoplasms has shown that bone destruction is always accompanied by the presence of two local factors — OAF and prostaglandins (PGs). Prostaglandins also act as endogenous mediators of cellular-mediated immune reactions and of production of lymphokines. It has been demonstrated that endogenous synthesis of prostaglandins is required for production of OAF. Evidently PGs are a necessary local mediator of cellular-mediated resorption of bone tissue: they are produced on the spot and have a short half-life period. PGs are essential for support of several types of cellular activity associated with bone tissue absorption. They increase activity of adenylate cyclase and enhance release of lysosomal enzymes. PGs must be released by monocytes for lymphocytes to produce OAF.

Other experiments have demonstrated the importance of increasing exchanges of membrane phospholipids for initiation of complement-dependent activation of cells. Evidently, this process is an essential early stage for stimulation of PGs synthesis and subsequent resorption of bone tissue.

It has recently been established that monokine IL-1, a humoral mediator of immune reactions which is a product of monocytes and macrophages, stimulates proliferation of lymphocytes *in vitro*. One of the nonlymphoid targets of IL-1 is bone tissue, which when exposed to a monocyte product with the properties of IL-1 is subject to osteoclast-dependent resorption in organic cultures. It has been hypothesized that IL-1 also participates in physiological resorption of bone tissue. It is argued that agents inducing osteoclast-mediated bone resorption do not act

directly on osteoclasts. Data suggest that resorption stimulators first act on another type of bone cell (evidently osteoblasts) which then activates resorption of bone tissue through osteoclasts and that IL-1 acts as an additional mediator here.

In 1980 the author put forth the hypothesis that OAF participated in the bone tissue resorption noted in hypokinesia and weightlessness. A number of working hypotheses that required empirical testing were advanced.

First it was proposed that the subpopulation of T-lymphocytes that synthesizes OAF may be the T-effectors of delayed hypersensitivity, since these are the cells that produces "lymphokines of inflammation". It has been found that weightlessness or its analog increases the activity of these cells. Whether changes in the balance between T-suppressors and delayed hypersensitivity T-effectors is associated with increased OAF production can be tested experimentally.

It has been established that in response to stress a portion of circulating lymphocytes migrates into bone marrow. It may be conjectured that this is the reason for decreased T-lymphocytes in the blood of cosmonauts. The second working hypothesis is that increased T-lymphocytes in bone marrow may result in local increase in OAF.

The third working hypothesis concerns an additional postulated function for OAF — that it acts to regulate the structure and metabolism of spongy bone.

Data in the literature support the conclusion that OAF, in conjunction with IL-1 and certain other factors, acts to support equilibrium between the osteoblast and osteoclast functions, determining the level of bone calcification (Figure 39). In response to long-term exposure to space or hypokinesia, changes occur in these functions, and in concentration and functional activity of a number of populations of immunocompetent cells, including producers of the majority of lymphokines and monokines. In addition, loss of calcium from bone tissue steadily increases. It has been proposed that these processes may be linked, and that one of the causes of disrupted calcium balance may be changes in certain components of the immune system. One effect that has been observed after space flight and hypokinesia is the increased activity of T-cell effectors of delayed hypersensitivity. It may be that this is associated with changes of T-suppressor control over these effectors.

It has been found that T-lymphocytes migrate to bone marrow in response to acute stress. Chronic stress on long-term space flights is a well-established phenomenon, and there are also periods of acute stress, for example, those associated with EVA. It can thus be assumed that during flight there are many periods in which T-cells undergo redistribution. It seems improbable that long periods of excess mature T-lymphocytes in bone marrow leave bone homeostasis unaffected. It is more likely that this situation would lead to local increases in level of OAF, and possibly other cytokines that participate in the regulation of bone resorption. This hypothesis requires experimental testing.

Finally, it has been proposed that a feedback loop exists in the system regulating cellular differentiation that determines the sizes of the zones or areas in which hemopoiesis occurs. Experiments with induction of osteopetrosis show how rapidly the composition of circulating cells in the blood can decrease the medullary cavities, and their filling with unresorbed endochondrial bone trabeculae. One can posit the existence of a factor that regulates structure and metabolism of spongy bone. OAF, IL-1, and other cytokines synthesized by immunocompetent cells are good candidates for such factors.

Initial studies directed at these hypotheses have involved investigation of production of OAF by lymphocytes in humans exposed to long-term hypokinesia and in splenocytes of animals flown

on biosatellites. OAF activity was measured in supernatant cultures of peripheral human leukocytes (or rat splenocytes) stimulated by mitogen during 48 hours at 37°. Culture liquid was added to organic cultures of long tubular bones of 19-day-old rat embryos or 17-day-old mouse embryos, tagged with ^{45}Ca . Resorption activity of OAF was estimated on the basis of release of ^{45}Ca from the bone tissue. In the long-term (120 days) hypokinesia study, OAF activity was measured in 15 subjects after bedrest varying in duration. The majority of these individuals periodically displayed elevated OAF activity. In a second study, production of OAF was investigated in 9 healthy males over a 240-day period of hypokinesia with head-down tilt. A large group of control subjects was used to determine the acceptable upper boundary for a resorption index obtained by comparing the supernatant activity of control and experimental cultures which was set as 1.6. In a baseline period the value of this index was 1.14 for all subjects. On day 60 of hypokinesia, the index was above the upper boundary of the norm for 4 of 7 subjects; on day 120 elevated indexes were obtained for 6 subjects. After 240 days, 8 out of 8 subjects studied showed resorption indexes above 1.6. Clinical studies revealed incipient periodontitis in 2 of these 8. All subjects showed increased excretion of calcium and its ionized fraction.

A third study established that probability of increased OAF production is a direct function of hypokinesia duration (at least for duration of up to 8 months). Since loss of calcium is well established, it is possible to hypothesize a connection between these two phenomena.

There is a general tendency in most, if not all, bones for activity of osteoclasts to increase under exposure to weightlessness and its analogs. This increases risk of local acceleration of resorption occurring due to inflammation neighboring tissues associated with accumulation of prostaglandins and other mediators that act as catalysts of OAF.

Changes in OAF production and immune parameters were compared in subjects in a 120-day hypokinesia experiment. After 2-3 months of bedrest, 5 out of 21 subjects displayed delayed hypersensitivity to bacterial allergens from normal human microflora. No effect of treatment was noted on natural killers. Five days before completion of 4 months of bedrest, index of cytotoxicity decreased. Concentration of T-lymphocytes did not change. PHA reactivity also remained normal in most cases, although some subjects displayed periodic moderate decrease in this parameter.

OAF activity in cosmonauts after flights and in animals flown on biosatellites is just beginning to be studied. Initial observations suggest the presence of changes analogous to those in long-term hypokinesia.

The author considers study of these phenomena a very promising area of space biology and medicine. Of particular interest is the hypothesis, for which some data exist, that the stress hormones (i.e., corticosteroids) may inhibit synthesis of PGE₂, which is essential for OAF formation, and thus slow resorption of bone tissue.

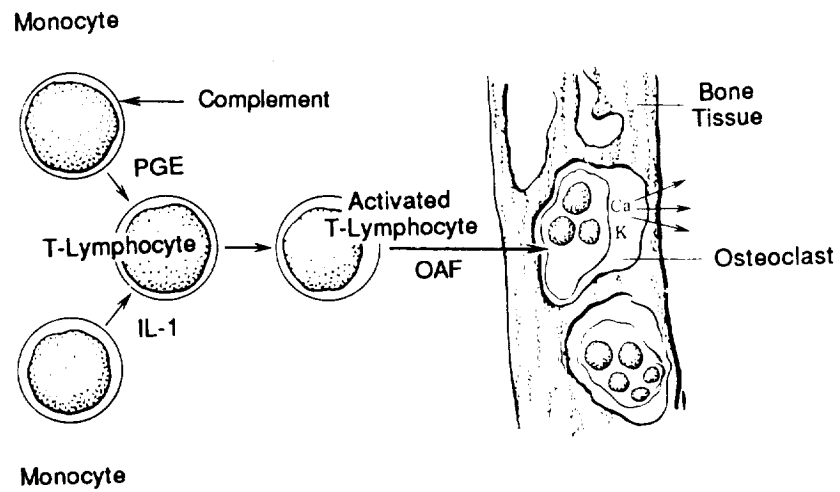


Figure 39: Diagram of cellular and humoral interactions preceding resorption of bone tissue mediated by OAF

P1171(25/89) Konstantinova, IV.

The human immune system: Effects of simulation of stress situations.

In: Konstantinova IV.

Sistema Immuniteta v Ekstremal'nykh Usloviyakh: Kosmicheskaya Immunologiya. Система Иммуитета в Экстремальных Условиях: Космическая Иммунология [***The Immune System Under Extreme Conditions: Space Immunology***] No. 59 in the series Problemy Kosmicheskoy Biologii. Проблемы Космической Биологии. [Problems of Space Biology]. Moscow: Nauka; 1988.
Pages 147-154.

Immunology

Humans

Psychology, Stress: Isolation

Abstract: This chapter reviews results of ground-based studies of humans exposed to psychological stress as evidenced by changes in biochemical parameters. In some cases stress was induced experimentally and in others naturally.

The pattern of change in parameters of immune reactivity was studied in two experiments, each of which lasted for 60 days. These experiments simulated a number of stress-inducing situations characteristic of space flight. A group of healthy males, no older than 40, were housed under comfortable living conditions with an optimal program of physical exercise and relaxation a fully balanced diet with controlled caloric intake. Periodically conditions were created associated with elements of risk and surprise designed to create emotional stress. The first of these conditions was simulated ascent in a hypobaric chamber to an altitude equivalent of 800 m. Subjects were warned one day ahead of time of the ascent, and ascent conditions were simulated, but apparently actual hypobaria was not produced. A second stress inducing factor was a warning that subjects were to undergo significant levels of acceleration several days in the future. A third situation involved psychomotor and logical task performance under time pressure in a pass/fail paradigm with public assessment of the intelligence of each participant. Ten subjects were studied multiple times in these two experiments. Venous blood was taken before beginning of the 60-day hospitalization period and then many times throughout the 2 months. When the subjects were warned about an upcoming situation, they were studied before and 1 day after the warning. A moderate decrease in T-lymphocytes (E-RFC) was found in one study during the period preceding the psychological test and during the anticipation period for acceleration. After the simulated barochamber ascent, T-lymphocytes decreased to a non-significant extent. Decrease in B-lymphocytes (EAC-RFC) occurred only after the psychological tests, while level of IgG+ increased.

The PHA reactivity of T-lymphocytes decreased sharply after the warning about acceleration treatment. This decrease was noted in all participants and in two, the parameter fell to 0. The barochamber condition led to decreased PHA reactivity of T-lymphocytes in three subjects. Levels of immunoglobulins remained unaltered, with the exception of IgA, which increased periodically in some subjects. Parameters normalized after the 60-day experiment.

Isolation experiments using hermetically sealed living quarters involve a baseline level of stress; acute stress may arise either through experimental manipulations or through other circumstances (e.g., interpersonal conflict) not under experimental control. In one 90-day experiment three individuals were isolated in an airtight living space 200 m³. Throughout the experiment microclimate parameters were held within recommended norms. Venous blood was taken for study of immune parameters on day 1 before isolation; on days 20, 30, 43, 57, 71, and 85 of treatment; and on day 13 of recovery. Soon after the experiment began an

interpersonal conflict for informal leadership of the group developed. Several weeks later another conflict arose between the subjects as a group and one of the support brigades. The greatest association between the stress situation and immune parameters was for cytotoxicity of natural killers. The greatest decrease (twice reaching 0) in cytotoxicity of natural killers occurred in the subject who played the main role in both conflicts. This same subject displayed the greatest increase in the stress hormones 11-oxy corticoid in blood and 17-KS in urine. A second subject showed increases of hydrocortisone and corticosterone in blood and decreased index of cytotoxicity at various times during the study. No changes were found in mean PHA reactivity of T-lymphocytes, but one subject showed reliable decrease at one point. Proliferative activity in a xenogenic graft vs. host reaction was unchanged for the group mean. However, two individuals did show a significant decrease in the proliferation index at certain points in the study. Group data for nonspecific suppressor activity also remained normal, but in one subject this parameter decreased at two points, while in another it fluctuated throughout the study. The two more passive participants in the conflict, showed a tendency for suppressor activity to decrease when the conflict began, while the active participant initially displayed elevation in this parameters followed by stable decrease.

In the second isolation experiment, three subjects spent 60 days in isolation in an airtight space 200 m³ under normal microclimate conditions. On days 7, 15, 28, 35, and 42, five "visiting crews" consisting of 2-3 individuals were placed in the quarters for a period of 5 days. When there were 5 or 6 people living in the space, CO₂ was allowed to increase to 2% for a period not exceeding 3 days. The conditions associated with the visiting crews placed additional strain on the original subjects. Use of acoustic communications and periods of sleep loss led to conflicts and deterioration of group interactions. At some points subjects had to work during the night hours. Blood was taken 16 days before the beginning of the experiment, four times during it, and twice in the recovery period.

Significant depression of suppressor activity of T-lymphocytes was found in all three subjects during the experiment. When individual data were examined points where the index of suppression was depressed corresponded to specific sources of stress. Cytotoxic activity of natural killers did not change significantly. Proliferative activity in a xenogenic host vs. transplant reaction was also not significantly altered.

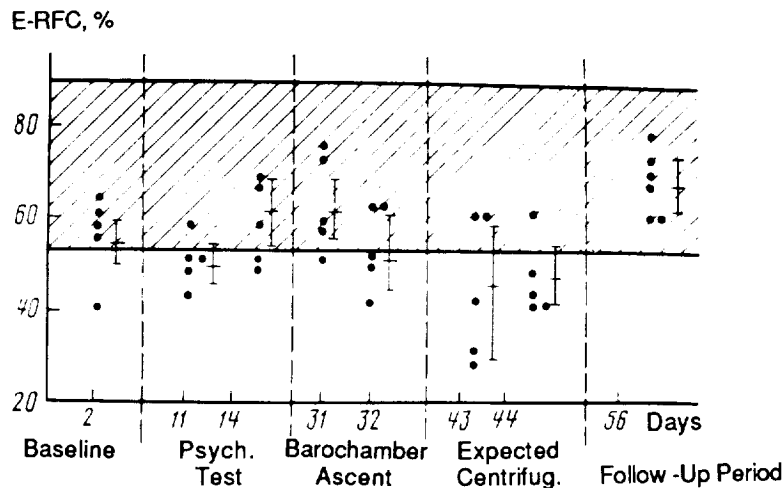


Figure 31. Concentration of E-RFC (%) in a 60-day study in which emotional stress was periodically induced

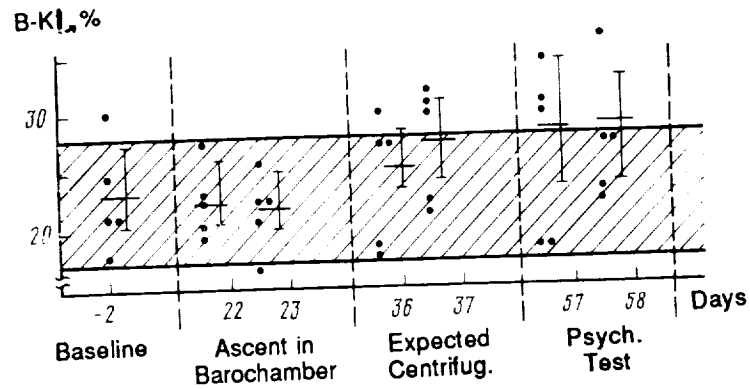


Figure 32: Concentration of B-lymphocytes (immunofluorescent method) in a 60-day study involving periodic induction of emotional stress

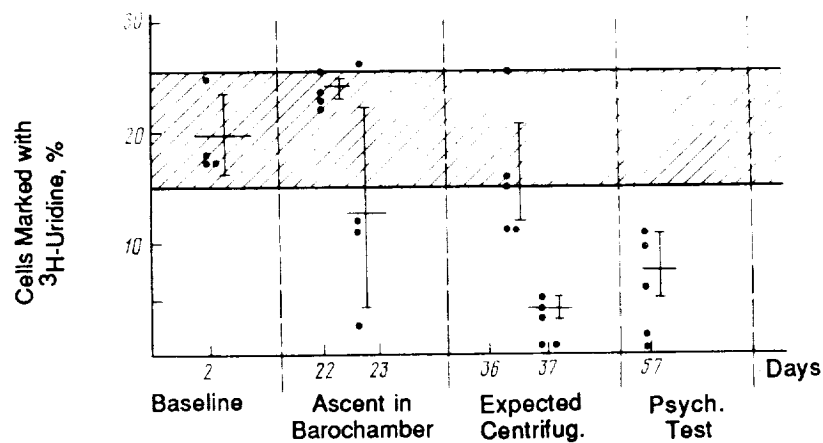


Figure 33: PHA reactivity of T-lymphocytes in a 60-day study involving periodic induction of emotional stress (individual and group values)

P1164(25/89) Konstantinova IV.

Space flight factors and the human immune system: Hypokinesia.

In: Konstantinova IV.

Sistema Immuniteta v Ekstrema'nykh Usloviyakh: Kosmicheskaya Immunologiya. Система Иммуитета в Экстремальных Условиях: Космическая Иммунология [***The Immune System Under Extreme Conditions: Space Immunology***] No. 59 in the series Problemy Kosmicheskoy Biologii. Проблемы Космической Биологии. [Problems of Space Biology]. Moscow: Nauka; 1988. Pages 125-146.

Immunity

Humans

Hypokinesia With Head-Down Tilt; Exercise; LBNP; Salt Supplements

Abstract: At the beginning of the 1960s, it was concluded on the basis of bedrest studies that hypokinesia decreases general resistance. The author and associates studied the dynamics of changes in immune response in ground-based studies modeling the effects of weightlessness using hypokinesia with head-down tilt. Immune status of healthy individuals was studied before, during, and after exposure to 182, 120, 120, 35, and 8 days of treatment. The first such study involved a 182-day period of hypokinesia and 18 healthy males divided into three groups. The first group was treated with a set of prophylactic measures similar to those developed for space flight, including physical exercise (twice a day for 60 minutes with energy cost of 350-400 cal/hr). The second group followed an abbreviated exercise program (20 minutes per day). Both groups were treated with lower body negative pressure and salt water supplements. No prophylactic measures were used for the third group. Two 120-day studies utilized 21 individuals, with a head-down tilt angle of 4.5°. Some of these subjects were treated with prophylactic measures. Six healthy women participated in the 35-day study. Of these, three engaged in a special set of physical exercises. Eight women participated in another 8-day study.

In the 182-day study, levels of E-RFC and EAC-RFC remained unchanged in all three groups. Eight individuals displayed a short-lived decrease in concentration of T-lymphocytes on day 40. Concentration of B-lymphocytes decreased moderately in 11 of 18 individuals during the first 1-1.5 months of treatment; this change was not associated with group membership. The 120- and 35-day studies had similar results. E-RFC level was depressed in some subjects on day 70 but then normalized. Other parameters were unchanged. PHA reactivity, which under normal conditions is quite labile, decreased in 15/18 subjects of the 182-day study, but only to a moderate extent. In this study certain subjects were affected by various minor ailments, boils, colds, periodontitis, etc. These ailments tended to coincide with the period of diminished PHA reactivity. Moderate decreased response to PHA was also found in the 120-day studies. Short-term (8-day) hypokinesia was not associated with decreased PHA reactivity.

Activity of natural killer cells measured using the Index of Cytotoxicity (IC) decreased during certain periods of hypokinesia. Study of individual patterns created the impression that there were two different response types. In some subjects decrease in IC occurred after 1-1.5 months of treatment, and continued to decrease until treatment stopped at the end of 4 months, normalizing after treatment terminated. In the minority of subjects, no changes occurred during treatment but cytotoxicity of natural killers decreased immediately after termination. In another study, cytotoxicity of natural killers decreased in five of eight female subjects on day 7 of an 8-day period of hypokinesia. Some women also showed decreased IC after treatment terminated.

Activity of T-helpers, estimated on the basis of the xenogenic graft vs. host reaction, underwent few significant changes. Nonspecific suppressor activity of T-lymphocytes was elevated during some periods of hypokinesia in some subjects, even during the shortest hypokinesia study.

Previous studies indicated that allergic hypersensitivity might develop during prolonged periods of hypokinesia. In the experiment imposing 182 days of hypokinesia with head-down tilt, the method of specific blastogenesis with a number of bacterial allergens, as well as skin tests with the same allergens, was used to determine allergic responses. Allergens used included staphylococcus, streptococcus, proteus, and intestinal bacilli. Tests of *in vitro* response of lymphocytes were performed six times for each subject

During hypokinesia, 7 of the 18 subjects displayed signs of developing sensitization to various bacterial allergens. The period preceding the appearance of positive reactions varied from 1.5 to 3 months. In four subjects, continued hypokinesia was accompanied by allergic response to additional allergens. There was no difference between subjects showing allergic sensitivity and those without such sensitivity with respect to number or duration of most bacterial or viral ailments developed during hypokinesia. Furuncles (boils) lasted significantly longer in subjects showing allergic sensitivity. When individual subjects were considered, a clear relationship was noted between the course of an ailment like boils and disruption of immune response. Tests using inhibition of leukocyte migration reaction as an indicator confirmed the occurrence of new allergic responses during the latter stages of a 120-day hypokinesia period in 8/21 subjects.

Table 4: Frequency and duration of ailments suffered by subjects during a 182-day period of hypokinesia with head-down tilt

Figure 23. Pattern over time of parameters of PHA-blastogenesis at various times during a 182-day period of hypokinesia in three subjects becoming ill three or more times during treatment

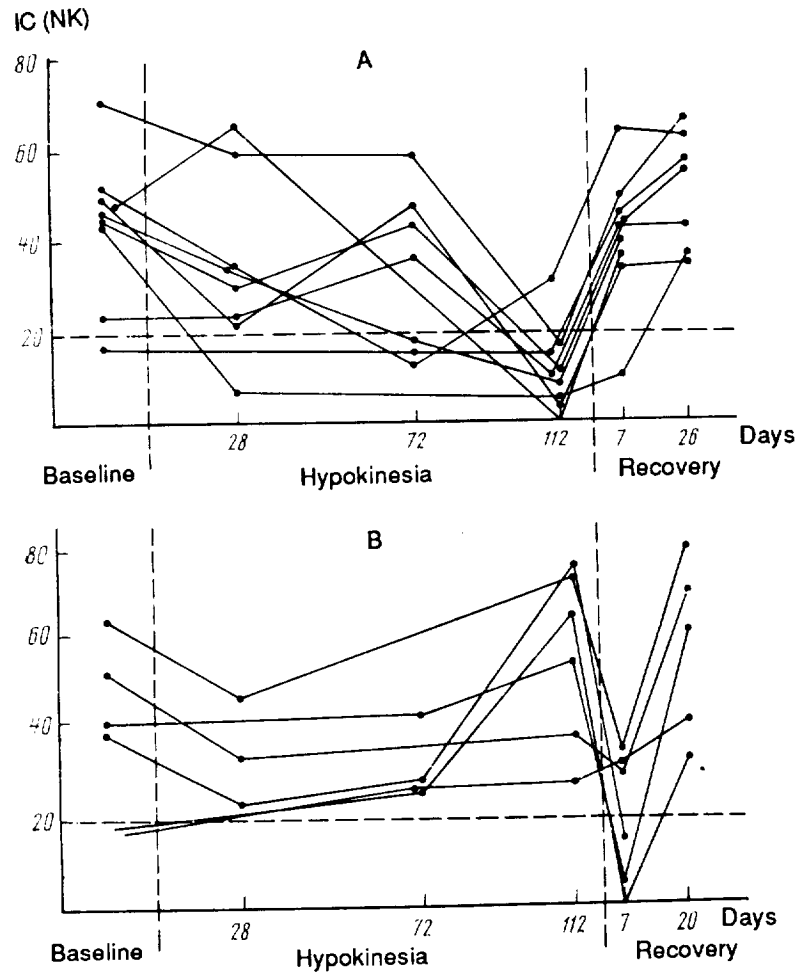


Figure 24: Changes over time in individual parameters of natural cytotoxicity of natural killers during a long (120-day) period of hypokinesia
 A - with decreased IC during hypokinesia, nine subjects; B - without decreases during hypokinesia, six subjects

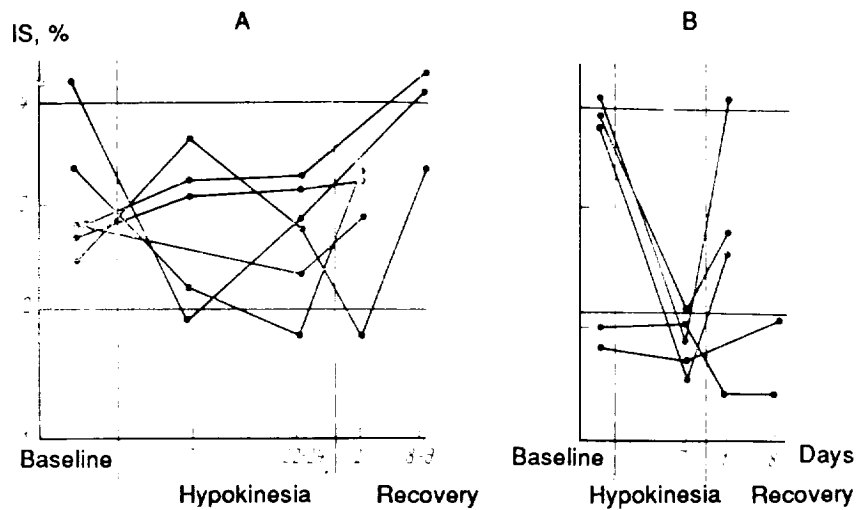


Figure 25: Changes over time in individual parameters of lymphocyte activity of T-helpers estimated using xenogenic graft-host reaction

A - 35-day hypokinesia; B - 8-day hypokinesia

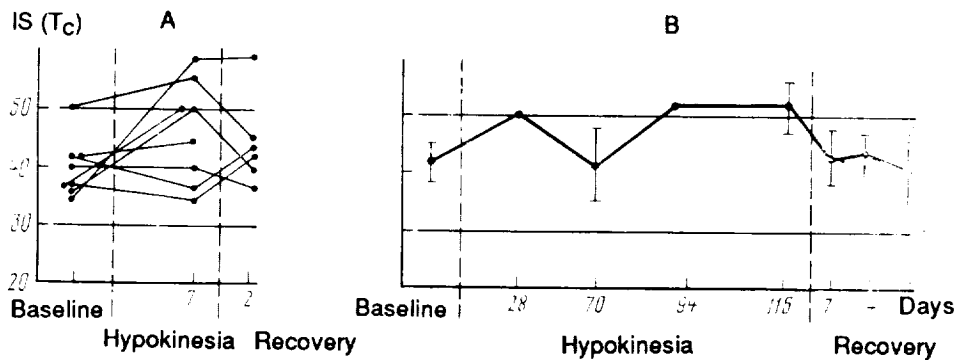


Figure 26. Nonspecific ConA-induced suppressor activity of lymphocytes in subjects

A - 8-day hypokinesia (individual data); B - 120-day hypokinesia (averaged)

Figure 27: Diagram of correlation in subject A throughout 182-day period of hypokinesia between presence of positive skin test to streptococcal allergen, sensitization to streptococci appearing on day 90 (specific blast transformation reaction) and development of illnesses

Figure 28: Correlation in subject M between signs of sensitization to streptococcus and staphylococcus, characteristics of staphylococcal microflora and development of illness during a 182-day period of hypokinesia

Figure 29: Correlation in subject S of occurrence of signs of sensitization to staphylococci and streptococci and development of illnesses during a 182-day period of hypokinesia

Figure 30: Sensitization to microbial allergens in five participants in an experiment involving 120 days of hypokinesia. Reaction of inhibition of leukocyte migration.

P1166(25/89) Lapayev EV, Azhayev AN, Kustova KA, Mar'yanskiy AA.

The effect of high environmental temperature on the thermal status and immunological reactivity of the human body.

Malkin VB, Kosmolinskiy FP, Kuznets Yel (editors).

Chelovek i Kosmos: Idei K.E. Tsiolkovskogo i ikh razvitiye v sovremennoy biomeditsine. Trudy

XXII Chteniy posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idej K.E.

Tsiolkovskogo (Kaluga, 15-18 sentyabrya 1987). Человек и Космос Идеи К.Э. Циолковского и их Развитие в современной биомедицине. Труды XXII Чтений; посвященных разработке научного наследия и развитию идей К.Э. Циолковского (Калуга; 15-18 сентября 1987)

Man and space: The Ideas of K.E. Tsiolkovskiy and their development in modern biomedicine.

Works from the XXII lecture series devoted to development of the scientific

heritage and development of the ideas of K.E. Tsiolkovskiy (Kaluga, 15-18 September, 1987)

Moscow: Soviet Academy of Sciences; 1988.

[72 pages; 6 tables; 2 figures]

Pages 38-41.

[7 references; none in English]

Immunology, Immunological Reactivity; Thermal Status

Humans

Heat

Abstract: This study investigated the effect of a single exposure to high environmental temperature on the major parameters of human immune status. Experiments were performed on eight subjects wearing summer clothes in a thermal chamber with air and wall temperature of 45°C. During the experiment the following parameters were measured: rectal temperature, skin temperature at five points on the body, pulse and respiration rate, blood pressure, and weight loss. Cellular immunity was studied by measuring percentage and absolute level of T-lymphocytes (reaction of spontaneous rosette formation, with sheep erythrocytes). Parameters of humoral immunity included relative and absolute concentrations of B-lymphocytes (rosette formation with mouse erythrocytes), and concentrations of major classes of immunoglobulins (A, M, G) in blood serum. The rosette-forming capacity of neutrophils was also assessed.

NOTE: Duration of exposure to heat is not given in the original.

It was found that exposure to the elevated temperature led to reliable increases in the absolute number of rosette-forming neutrophils and B-lymphocytes. There was also a tendency for the absolute numbers of neutrophils and lymphocytes to increase.

At the termination of exposure, rectal temperature had risen by 1.2°, pulse had increased by 35 beats per minute, and weight loss constituted 2,114 g. All increases in immune response noted on day 1 after treatment had virtually normalized by day 3 after treatment.

LIFE SUPPORT SYSTEMS

PAPERS:

P1143(25/89)*Shikina MI, Aladinskaya TI, Volkova LN, Duplik AZ.

Artificial mineralization of desalinized potable water with salt tablets and powders.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 74-76; 1989.

[6 references; none in English]

Life Support Systems, Desalinized Potable Water

Humans

Salt Tablets and Powders

Abstract: Solubility of salts (sulfate, gluconate, carbonate) in desalinized water was studied at room temperature. The time required for suspension of calcium to dissolve in the water (with and without stirring) was evaluated and the transparency and concentration of calcium ions determined. Tablets were formed from salt powders containing calcium salts combined with magnesium sulfate, potassium iodide, potassium chloride, and sodium fluoride. Other substances — starch, polyvinylpyrrolidone, methyl cellulose, and potassium stearate — were used as fillers to increase the adherence of the powders into tablets. After mixing the fillers and salts, the mixture was dried and sieved. Tablets were produced by an impact tablet machine.

Results showed that CaCO_3 was not suitable for artificial mineralization of water due to low solubility. The most soluble compound was calcium gluconate, but this salt allowed the water to remain transparent only when combined with methyl cellulose. Dissolution time of this substance was 35 minutes. However, calcium gluconate increased the bichromate oxidizability of the water, which did not accord with hygienic standards for potable water. Dissolution time of calcium sulfate in water was 60-80 minutes with stirring and 6 hours without it. This substance did not affect bichromate oxidizability (chemical absorption of oxygen). This substance was considered most suitable to be included in the salt mixtures along with sodium chloride, potassium chloride, magnesium sulfate, potassium iodide and sodium fluoride for mineralizing desalinized water. A tablet (Akvasol-2) was prepared from these salts, which dissolves in water in 12 hours without stirring. This tablet is recommended.

Table 1: Results of research on artificial mineralization of water with powders

Table 2: Results of research on artificial mineralization of water using tablets

MONOGRAPH:

M150(25/89) Troshikhin GV.

Organizm v gelio-kislorodnyy srede (Организм в гелио-кислородной среде) [***The organism in a helium-oxygen atmosphere.***]

Leningrad: Nauka; 1989.

[157 pages; 12 Tables; 24 Figures; 477 references]

KEY WORDS: Life Support System, Biological Effects; Hypoxia; Hyperoxia; Warm Blooded Animals; Biospherics, Helium Atmospheres; Altered Oxygen Pressure

Annotation: A substantial portion of this book is devoted to the author's research on the mechanism underlying the physiological effect on warm-blooded animals of helium atmospheres with varying concentrations of oxygen at atmospheric pressures. Literature on the effects of such atmospheres on humans and animals is also summarized.

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The functional state of warm-blooded animals in a normoxic helium atmosphere (15)

The physiological effect of hyperoxic helium atmospheres at atmospheric pressure (20)

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Research methods (25)

Experimental animals (27)

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CONCLUSION

The evolution of life on Earth took place in a nitrogen-oxygen atmosphere and vertebrates evolved in a atmosphere that had the same gaseous composition that exists today. For this reason higher animals and man are adapted to breathe air, their natural living environment. At the same time, they can tolerate relatively long periods in an altered atmosphere at atmospheric pressure that contains other inert gases, especially helium, without major disruptions of physiological processes. Naturally, the differences between the physical properties of helium and nitrogen induce certain shifts in the body. As a result of helium's low density, respiratory resistance decreases and afferent stimulation from the mechanoreceptors of the lungs and chest cage decrease, leading to increased respiration rate and decreased depth. Due to the high thermal conductivity of helium, heat loss increases, leading to an increase in heat production. The latter may be eliminated by increasing the temperature of the environment and keeping it strictly within the comfort zone. At the same time, when atmospheric nitrogen is replaced by helium at comfortable temperatures, tissue ultrastructure, especially that of the lungs, which is in direct contact with the gas, and metabolic processes at the cellular level, especially metabolism of the mitochondria of the cerebral cortex, do not alter. It is true that these conclusions are known to hold only for a relatively short exposure (several days or less) to a helium-oxygen atmosphere. The, limited amount of experimental research with prolonged exposures has not yet made it possible to extrapolate findings to a longer period. However, judging by the data in the literature, a normoxic helium-oxygen atmosphere may be used in the living environment for periods as long as several months. Of course, the shift and narrowing of the zone of thermoneutrality in this atmosphere introduces certain problems associated with the need to maintain a strict temperature schedule.

If we speak of the adequacy of an atmosphere, then we should remember that, as a result of many million years of evolutionary development and natural selection, the bodies of animals have gradually developed properties adapting them to the conditions under which they live. Any changes in the composition of the natural atmosphere, especially the concentration of oxygen in the environment, will introduce alterations in the functioning of one or another physiological system. Changes in atmospheric oxygen within small limits (approximately 3-5% in either direction) do not evoke any changes in the systems responsible for supplying oxygen to the tissues, since these systems have a "margin of safety" and do not react to small deviations. However, decrease in atmospheric oxygen to 17-16% induces intensification of external respiration compensating for the inadequate oxygen supplied to the body.

Adaptive responses to hypoxia are a result of the entire process of evolution, since the organism constantly encountered situations in which increased expenditure of energy was required for survival. Hyperoxia is a another matter, since it is a situation the organism did not encounter during evolution. The organism had to fight for oxygen and expend additional energy to obtain it, but it never had to limit its intake. Thus, terrestrial animals do not have effective physiological reactions directed at decreasing the supply of oxygen or excreting the excess.

At the same time, when concentration of oxygen increases in the atmosphere up to 33-35%, the natural hypoxic stimulation from peripheral chemoreceptors is eliminated. This in itself disrupts the physiological conditions characteristic of normal functioning of the respiration regulation system, and thus such an atmosphere cannot be considered appropriate for the organism. Further increase in concentration of atmospheric oxygen up to 40-60% initially increases the level of metabolic processes, and then depresses it. However, an atmosphere that

artificially activates redox processes in the body cannot be considered optimal since stimulation of metabolism is unavoidably associated with a certain strain on many enzyme systems and may lead to functional disruptions and early breakdown of organelles responsible for energy supply. It is another matter when the artificial atmosphere stimulating or inhibiting metabolic processes is used in the clinic for treatment of certain diseases. In such situations one should speak not of the optimal level of oxygen in the atmosphere, but about a nontoxic level at which its adverse effects on the organism are not yet in evidence.

In certain specific situations, oxygen pressure may have to be increased in the breathing medium. Oxygenation of the atmosphere in the inhabited modules of a spacecraft may increase crew survival time in emergency situations and thus increase opportunities for fixing a malfunction, and also serve as a prophylactic measure to prevent decompression sickness associated with EVA. A patient may need to breathe hyperoxic media for days at a time. For these reasons it is essential to determine the nontoxic concentration of oxygen in the atmosphere for both short- and long-term human exposure. The author's research shows that 60% concentration of oxygen, combined with nitrogen or with helium, has a toxic effect on the organism for exposures of 2-5 days, while toxicity occurs even sooner with 80% oxygen atmospheres. It should also be remembered that signs of oxygen toxicity occur sooner when this gas is mixed with helium than with nitrogen. However, for short-term inhalation the use of a 60-80% oxygen-helium media is permissible.

Analysis of data in the literature and of our own experimental results suggests that a 40% concentration of oxygen in helium, as well as nitrogen, mixtures is the limit at which minimal signs of adverse effects of oxygen begin to be felt under conditions of long-term exposure.

While helium-oxygen atmospheres are still not used in cosmonautics, recently they have been more extensively introduced in clinical practice for diagnostic purposes and as an effective therapeutic measure. The use of hyperoxic helium mixtures is particularly promising. Excess concentration of oxygen is the most effective factor for curing hypoxia of various etiologies, and the introduction of helium into the breathing mixture not only decreases respiratory resistance, but improves the functioning of diffusive processes in the lungs and tissues. Obviously, special inhalation schedules with duration and breathing mixture composition determined by vital signs and etiology, will have to be developed for various illnesses.

MATHEMATICAL MODELING

PAPERS:

P1133(25/89)* Astanin SV.

An integrated approach to modeling the functional state of a human operator based on the theory of fuzzy sets.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 29-33; 1989.

[3 references; none in English]

Human Performance, Functional State

Humans, Operators

Mathematical Modeling, Fuzzy Sets, Man-Machine Systems

Abstract: This paper purports to take a systems approach to the concept of functional state, conceived as a complex psychological phenomenon arising from the interaction of all the physiological systems pertinent to operator performance. This involves analyzing information flow within a man-machine system to identify the components of the internal and external environment.

Figure 1: Example of types of interactions among the elements of a man-machine system

Figure 2: Representation of the dominance relationships using fuzzy matrices

Figure 3: Example of construction of a man-machine system structure based on fuzzy matrices

P1145(25/89)* Mazurin YuV, Stupakov GP.

Predicting the effects of linear and angular impact acceleration on humans.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 79-83; 1989.

[4 references; 1 in English]

Mathematical Modeling, Physiological Effects, Prediction
Humans
Acceleration, Linear, Impact

Abstract: The goal of this work was to develop a computer-based method for predicting probability of physiological damage, as well as more subtle effects such as changes in operator performance level after exposure to linear and angular impact acceleration, characteristic of extreme or emergency flight conditions. The model proposed is based on establishing statistical associations and functional relationships between biomechanical and other effects and parameters of the response of a mathematical model of the human body, expressed as a vector of reactions. These reactions serve as an intermediate variable between impact parameters and physiological effect parameters. The only requirement for predicting effects using this approach is the presence of statistically significant associations between the reactions of the mathematical model and the effects being evaluated.

The authors argue that their method for predicting the effects of linear and angular impact acceleration makes it possible to expand the range of predictions, and evaluate the acceptability of a complex factor. In addition it has the flexibility to permit statistical processing of biomedical information and mathematical modeling in the interest of ensuring safety and required performance levels in crewmembers subject to impact acceleration.

Figure 1: Structure of prediction of trauma risk and other effects of linear and angular impact acceleration

Figure 2: Computational structure of the model

Figure 3: Diagram of the model of the head and neck and area of maximal angular deviations of the head

Figure 4: Changes in the area of acceptable values of linear acceleration

METABOLISM

PAPERS:

P1134(25/89)* Delenyan NV, Markin AA.

State of the lipid peroxidation system in the tissues of rats after a 7-day flight on COSMOS-1667.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 34-37; 1989.

[20 references; 9 in English]

Metabolism, Lipid Peroxidation

Rats

Space Flight, COSMOS-1667

Abstract: The goal of this experiment was to measure the concentration of products of lipid peroxidation (diene conjugates, Schiff bases, malonic dialdehyde), as well as the activity of the major antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase), and the important bioantioxidant tocopherol in the tissues of rats exposed to space flight. A study was performed on four groups of Wistar rats. Group 1 was the flight group, flown for 7 days on COSMOS-1667. Group 2 was the vivarium control for the flight group. Group 3 was the synchronous control and Group 4 was a second vivarium control. Each group contained seven rats. The animals were decapitated 4-6 hours after touchdown. Samples of liver tissue, the posterior muscles of the femur, and the myocardium were washed in a cold saline solution and frozen in dry ice. The tissues were homogenized. Activity of superoxide dismutases was measured by an undescribed method. Glutathione peroxidase activity was estimated in a conjugated glutathione reductase system using hydrogen peroxide as substrate. Activity of glutathione reductases was estimated from oxidation of NADP/H. Catalase activity was estimated by an undescribed method. For full extraction of intracellular enzymes, the tissue homogenates were processed with triton X-100 in a terminal concentration of 0.1%. The concentrations of diene conjugates, tocopherol, and Schiff bases were measured, as was protein concentration. Concentration of total lipids was measured using the phosphovanillin method. Data were analyzed statistically using t-tests.

The myocardium of flight rats displayed a reliable elevation in superoxide dismutase activity compared to the synchronous and vivarium controls. The absence of significant differences in the activity of glutathione peroxidases, glutathione reductase, and catalase suggests only a slight intensification of free-radical processes in the myocardium. The concentration of tocopherol was elevated in the myocardium of both the flight and synchronous groups, which is interpreted as resulting from a compensatory process. No reliable differences were found in the muscle tissue of flight rats, with the exception of a reliable decrease in glutathione peroxidase activity. In the livers of flight animals, the concentration of diene conjugates increased by 33%, that of malonic dialdehyde by 30%, and that of Schiff bases by 24%. In addition, superoxide dismutase activity was elevated, while activity of glutathione peroxidase was depressed. Tocopherol concentration was elevated by 57%. The synchronous group was no different from the control. These results are interpreted as demonstrating that the 7-day space flight led to a generalized intensification of lipid peroxidation in the liver of flight rats. Antioxidant compensatory response to these changes did not appear adequate.

METABOLISM

Table 1: Activity of enzymes providing antioxidant protection in rat tissues

Enzyme	Flight (7)	Vivarium Control (14)	Synchronous Control (7)
Superoxide dismutase, unit per 1 mg protein			
myocardium	15.38±1.28*	10.33±0.95	11.8±0.2
muscles	8.6±0.75	8.6±0.92	11.5±1.5
liver	40.1±1.6*	35.1±1.6	38.2±1.8
Glutathione peroxidase, nmole/min per 1 mg protein			
myocardium	16.0±3.6	19.9±1.8	21.2±5.3
muscles	4.1±0.11*	5.3±0.28	4.8±0.39
liver	15.3±1.66	23.5±1.6	25.7±1.65
Glutathione reductase, nmole/min per 1 mg protein			
myocardium	5.3±1.6	7.7±1.1	7.6±1.1
muscles	2.5±0.3	2.3±0.1	2.7±0.31
liver	14.3±5.3	14.3±5.4	14.3±0.57
Catalase, units/sec. per 1 mg protein			
liver	0.1±0.008	0.11±0.005	0.094±0.005

Here and in Tables 2 and 3 * difference from vivarium control reliable, $p < 0.05$. Number in parentheses refers to number of subjects

Table 2: Concentration of tocopherol (in mg per 1 mg lipid) in tissues of rats

Tissue	Flight	Vivarium	Synchronous
Myocardium	1.12±0.15*(6)	0.74±0.05(7)	1.02±0.06(6)
Muscles	0.30±0.07*(6)	0.59±0.08(13)	0.83±0.21(7)
Liver	0.77±0.07*(7)	0.49±0.08(14)	0.70±0.05(6)

Table 3 Concentration of lipid peroxidation products in the tissues of rats

Parameter	Flight	Vivarium 1	Synchronous	Vivarium 2
Diene conjugates, μ equiv per 1 mg lipids				
myocardium	$3.81 \pm 1.31(6)$	$2.95 \pm 0.31(7)$	$1.57 \pm 0.03(6)$	---
muscles	$4.13 \pm 0.75(7)^{**}$	$2.47 \pm 0.32(6)$	$1.78 \pm 0.18(6)$	$3.23 \pm 0.11(7)$
liver	$1.78 \pm 0.08(7)^{***}$	$1.34 \pm 0.06(6)$	$1.55 \pm 0.07(7)$	$1.82 \pm 0.05(7)$
Malonic dialdehyde, nM per 1 g tissue				
myocardium	$110.4 \pm 7.8(7)$	$117.8 \pm 4.4(13)$	$116.7 \pm 11.9(5)$	----
muscles	$163.7 \pm 15.1(7)^{**}$	$125.2 \pm 12.6(14)$	$96.2 \pm 6.6(7)$	----
liver	$208.6 \pm 20.3(7)^{***}$	$160.3 \pm 6.8(14)$	$113.6 \pm 3.0(7)$	----
Schiff bases, units per 1 mg lipid				
myocardium	$196.0 \pm 19.3(6)^{**}$	$229.3 \pm 11.5(7)$	$257.4 \pm 6.2(6)$	----
muscles	$13.02 \pm 2.7(7)$	$15.32 \pm 2.66(6)$	$9.88 \pm 1.01(7)$	$28.65 \pm 1.98(7)$
liver	$241.6 \pm 14.6(7)^*$	$194.9 \pm 6.4(6)$	$235.9 \pm 12.1(7)$	$262.7 \pm 12.8(6)$

****** significantly different from synchronous control, $p < 0.05$; ******* significantly different from both synchronous and vivarium controls

P1138(25/89)* Popova IA, Vetrova YeG, Drozdova TYe.

The effect of long-term hypokinesia with head-down tilt on activity of enzymes participating in energy and anabolic metabolism.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 51-55; 1989.

[14 references; 2 in English]

Metabolism, Energy (Catabolic), Anabolic, Enzymology

Humans, Males

Hypokinesia With Head-Down Tilt; Long-Term; Pharmacological Countermeasures, Physical Exercise

Abstract: Nine healthy male volunteers participated in this study, involving 370 days of hypokinesia with head-down tilt (-5°). Group 1 (n=4) received a number of prophylactic measures, including pharmacological countermeasures directed at normalization of fluid-electrolyte, mineral, lipid, and calcium metabolism and pancreatic function, as well as physical exercise in a horizontal position. Group 2 subjects (n=5) were given the countermeasures after 4 months of hypokinesia. Blood was taken for study from the radial vein on an empty stomach, during a baseline period, on days 50, 110, 170, 230, 300, and 350 of treatment, and on days 1 and 7 of the recovery period. Standard optimized methods were used to determine activity of enzymes belonging to the following classes: 1) oxidoreductases (lactate dehydrogenase /LDH/, malate dehydrogenase /MDH/, isocitrate dehydrogenase /ISDH/, glutamate dehydrogenase /GDH/); and 2) transferases (alanine aminotransferase /ALT/, aspartate aminotransferase /AST/, γ -glutamyl transferase / γ -GT/, creatine phosphokinase /CPK/). Total activity of the isoenzymes of LDH of the H-type characteristic of tissues with high levels of aerobic metabolism, especially cardiac tissue, was measured by determining activity of α -hydroxybutyrate dehydrogenase (α -OBDH). Isoenzymes of muscular CPK (M-CPK) and myocardial CPK (MC-CPK) were measured using the method of selective activation. Statistical analysis was performed.

Patterns of change over time were different for each enzyme. LDH was significantly above baseline on day 110 and depressed on day 1 of recovery for both groups. α -OBDH was elevated during treatment, except for days 300 and 350 for both groups and on day 7 of recovery for group 2. MDH did not differ from baseline except for elevation on day 350 of treatment for group 2. ICDH was depressed sporadically throughout treatment and recovery for both groups. GLDH did not differ from baseline, with the exception of decrease on day 300. CPK was depressed in group 2 and elevated in group 1 on day 50, with the intergroup difference being statistically significant. Activity of CPK and its isoenzymes was elevated in both groups during the early part of recovery. This effect was particularly marked in group 2, which contained two subjects with elevated baseline levels of this enzyme. Transferases tended to react to the treatment by moderate elevation. ACT levels were depressed for group 2, but not group 1 during the last portion of the hypokinesia period and the initial recovery period.

The authors consider the most important results to be as follows: a 370-day period of hypokinesia with head-down tilt led to a decrease of the activity of serum ISDH, CPK, and GDH, and an increase in activity of ALT, AST, γ -GT and also LDH (due to the H isoenzyme).

Countermeasures had a corrective effect only for CPK, γ -GT, and ACT, with the latter observed only when prophylactic measures were applied throughout.

The authors point out that the enzymes whose activity was altered by the treatment are mainly participants in energy (catabolic) metabolism. Decrease of CPK and ISDH in blood may be explained by decreased energy metabolism in tissues, especially those of the skeletal muscles.

Due to decreased activity of Krebs cycle enzymes, and also CPK, the oxidation of substrates slows and the proportion of ATP forming from creatine phosphate diminishes. In tissues with aerobic metabolism, such as the myocardium, the role of glycolysis simultaneously increases, as shown by the parallel increase in activity of LDH. Increased activity of transaminase in blood may be explained by utilization of amino acids as energy-producing substrates, since their availability in blood increases during hypokinesia due to decomposition of tissue proteins accompanied by inhibition of anabolic process; and by the need for compensatory activation of gluconeogenesis given the hypoglycemia characteristic of later stages of hypokinesia. It is noted that the prophylactic countermeasures had only partial corrective effects and did not maintain energy metabolism processes at a normal level.

Table 1: Activity of serum enzymes in group 1

Table 2: Activity of serum enzymes in group 2

P1139(25/89)* Tolkacheva NV, Levachev MM, Medvedev FA, Lupinovich VA, Sorokina AG.
Binding of fatty acids and products of their peroxidation by serum albumin under conditions of strenuous exercise.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 55-59; 1989.

[21 references; 7 in English]

Metabolism, Fatty Acids, Binding
 Humans, Athletes, Nonathletes
 Exercise, Strenuous

Abstract: The objective of this paper was study of the binding of serum albumin to total lipids, fatty acids and products of their peroxidation in subjects (long-distance bicyclists) undergoing highly strenuous exercise. Subjects were 22 individuals, aged 17 to 25, variously ranked (master and first class) as bicyclists, undergoing a moderately strenuous training schedule. The control group contained 42 nonathletes. Serum albumin was isolated by electrophoresis in a polyacrylic gel. Purity of the albumin was evaluated using disk-electrophoresis. Concentration of protein was measured using the biuret test. Lipids bound with albumin were extracted. The fatty acids of the extract were methylated with acetyl chloride. A gas chromatographic analysis of the fatty acid esters thus obtained was conducted using a flame-ionization detector. Identification of fatty acids utilized comparison of the volumes retained in the mixture with standard preparations of methylated ester of saturated and unsaturated fatty acids from C₁₂ to C₂₄. Internal standardization was used to determine the relative quantities of fatty acids, and individual fatty acids were expressed in percentages of the total. Concentration of total lipids was determined. Concentrations of products of lipid peroxidation — diene conjugates and ketones — were measured. Blood was taken from the cubital vein before and after exercise in the long-distance bicyclists during the recovery period of the training cycle.

In the baseline condition, athletes' blood contained a significantly higher concentration of total lipids bound by serum albumin than that of nonathletes, suggesting that exercise increases albumin's binding capacity. Exercise increased binding capacity in both groups of athletes, but to a greater extent in the more proficient ones, indicating greater metabolic restructuring. Percentage of linoleic and arachidic fatty acids bound by albumin after exercise was significantly lower in the highly qualified athletes than in the moderately qualified ones, suggesting that in the former the metabolic transformation of linoleic acids into arachidic was intensified, possibly with subsequent synthesis of prostaglandins (E₂, E_{2α}). Before exercise, athletes' blood contained a higher proportion of eicosapentaenic acid, than that of nonathletes. This acid acts as a substrate in synthesis of the prostaglandins E₃, E_{3α}, and I₃ and thromboxane A₃, preventing aggregation of thrombocytes. After exercise this acid decreased to a greater extent in the more qualified athletes. Diene conjugates and ketones were less numerous in the blood of moderately qualified athletes than in the control group. These substances were present only in trace amounts in the "master" athletes.

The authors argue that serum albumin plays an important role in the transport of polyunsaturated fatty acids and products of their peroxidation, serving to support adaptive restructuring of metabolism in response to strenuous physical exercise in athletes.

Table 1: Concentration of lipids and products of lipid peroxidation in serum albumin in long-distance bicyclists during the recovery period of their annual training cycle

Table 2: Concentrations of fatty acids bound by serum albumin in athletes before and after physical exercise

P1150(25/89)*Potapov PP.

Rate of glycolysis and glyconeogenesis in skeletal muscles of rats during readaptation after hypokinesia of up to 30 days.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 92-94; 1989.

[13 references; none in English]

Metabolism, Glycolysis, Glyconeogenesis; Musculoskeletal System, Skeletal Muscles
Rats
Hypokinesia, Readaptation

Abstract: Experiments were performed on 68 white rats, of which 58 were maintained in immobilization cages for either 15 or 30 days. After termination of immobilization, animals were placed in common cages. Selected animals were sacrificed at termination of the hypokinesia period and at daily intervals up to 20 and 28 days, respectively for the 15- and 30-day condition. The method of moving averages was used to investigate the time course of the parameters studied, and the Mann-Whitney-Wilcoxon nonparametric test was used to determine statistical significance. Skeletal muscle tissue (from the posterior group of femur muscles) was extracted in cold, homogenized, and centrifuged for 40 minutes. Glycolysis rate was determined from a medium containing protein, a potassium phosphate buffer, nicotinamide, NAD and either glucose, glucose-6-phosphate, or glycogen. Concentrations of lactate and protein were measured.

In control animals, rate of glycolysis on glucose and glucose-6-phosphate equalled 15.9 and 56.4 nmoles lactate per minute on 1 mg of protein; rate of glyconeogenesis was 39.6 nmole lactate per minute for 1 mg protein. On day 15 of hypokinesia the rate of the process on all three substrates was elevated. On day 30 rate of glycolysis on glucose was below the norm, while lactate production was significantly elevated on glucose-6-phosphate and glycogen. The author argues that these data suggest that in long-term hypokinesia the preferential use of fat as a source of energy is due not to attenuation of the enzyme system of carbohydrate oxidation, but to a lack of substrate. After the 15-day hypokinesia period, the rate of dichotomic decomposition of carbohydrates rapidly decreased, starting on day 2 or 3 of recovery. The statistically significant inhibition of glycolysis on both substrates continued until day 11 of recovery. Rate of glyconeogenesis normalized on day 9. After the 30-day hypokinesia period, rate of glycolysis on glucose was significantly depressed from days 5 to 17. With glucose 6-phosphate as the substrate, lactate formation first remained elevated and then began to decrease on day 6, remaining below the norm until day 17. Rate of glyconeogenesis was also depressed during this period. Between days 21 and 23 of readaptation, rate of lactate formation on glucose 6-phosphate and glycogen was significantly elevated. Since the limiting enzyme in muscle tissue glycolysis is hexokinase, while phosphorylase plays this role in glyconeogenesis, and , rate of lactate formation depends on phosphofructokinase when glucose 6-phosphate is the substrate, it can be conjectured that the activity of these enzymes was depressed during the early readaptation period. However, since lactate formation was most depressed on glucose 6-phosphate, it can be concluded that phosphofructokinase was the limiting factor. The depression of glycolysis and glyconeogenesis found in this study are likely to be important in the excess accumulation of glycogen in skeletal muscles in the early recovery period after hypokinesia.

Figure 1: Change in the rate of formation of lactate from glucose, glycogen, and glucose 6-phosphate in the skeletal muscles of rats in the recovery period after a 15-day period of hypokinesia

Figure 2: Change in the rate of formation of lactate from glucose, glycogen, and glucose 6-phosphate in the skeletal muscles of rats in the recovery period after a 30-day period of hypokinesia

MICROBIOLOGY

PAPER:

P1135(25/89)* Volz PA.

Fungal experiments in outer space.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 37-43; 1989.

[56 references; 50 in English]

Microbiology, Fungi

Yeast, Conidia, Ascospores

Space Flight, Apollo; Radiobiology, Solar Radiation

Abstract: This paper describes results of U.S. microbial investigations on Apollo flights. Somatic cells of yeast, conidia and ascospores of four selected species of fungi were housed in the Microbial Ecology Evaluation Device (called in Russian: Microbiological Device) and exposed at an angle of 90° to the Sun for 10 minutes plus 7 seconds in open space during an EVA. The fungi had been selected for survival in the conditions associated with the onboard apparatus, and on the basis of their suitability for evaluation of the cellular effects of space flight, existence of previous experimental data, and ease of maintenance in flight. The selection process took 2 years. The flight samples were housed in cuvettes containing a fixed number of fungal cells, either dry or suspended in water. Each cuvette had a quartz window, one bandpass, and one neutral density light filter, so that the samples could be selectively irradiated with UV solar radiation components. The cells were exposed to UV radiation with wavelengths of 254, 280, and 300 nm varying in energy, and also to sunlight; a control sample remained in the dark. Some cuvettes with dry samples were exposed to the vacuum of space. Control experiments were performed on Earth at room temperature, onboard the station in darkness and also in various NASA experimental set-ups simulating maximal levels of the space flight factors of vibration and solar radiation. After spacecraft splash-down, the devices were delivered to the NASA Lunar observatory. Samples of the flight subjects were isolated and placed on an agar substrate for further study. Flight and control samples were compared for viability, macroscopic, microscopic, and physiological changes.

Fungi viability was not affected by weightlessness or dynamic flight factors. Nevertheless, survival duration, and consumption of nutrients varied as a function of flight factors. Rate of consumption of phosphate by cells of *S. cerevisiae* postflight was approximately twice that of control, possibly due to altered physiology of the cell membranes. The greatest change in lipid synthesis and phospholipids was obtained in cells of *R. rubra* after irradiation in space with UV rays 254 nm in wavelength. *C. globosum* cells exposed to space manifested altered nuclei shapes. A single isolate showed enhanced effects to repeated UV-irradiation, but the remaining cells displayed no additional changes. Flight cultures of *S. cerevisiae* introduced into wounds of animals showed greater capacity for recovery than nonflight cells and this difference persisted for 7 years. All flight cultures of yeast exposed to UV irradiation and maintained in darkness in space showed enhanced sensitivity to test drugs. Flight samples of *T. terrestris*, parasitic on human hair, were less effective than control samples. *C. globosum* fungi, which have cellulolytic capacity, lost the capacity to produce pigment, and underwent other changes after space flight combined with UV radiation. Percent of survival was lower for flight cultures.

Flight and ground cultures of *C. globosum*, *T. terrestris*, *R. rubra* and *S. cerevisiae* were introduced into samples of saliva from healthy individuals and three groups of patients. The flight cultures showed impaired growth in the presence of peroxidases in the saliva of patients undergoing radiation therapy, or taking steroids or insulin. The genomes of flight cultures of *C.*

Colobosum and *T. terrestre* displayed greater numbers of both pairs of nucleotides per haploid nuclei. Size of genome was elevated postflight for these fungi. Exposure of *T. terrestre* to flight factors altered concentrations of phospholipids in the cells. Flight phenotypes of all four species of fungi displayed morphological differences compared to controls, mainly in the structure of the hypha, development of colonies, and shape of the cells. Postflight studies suggested that changes in fungi cultures were due to damage to individual cells by space flight factors.

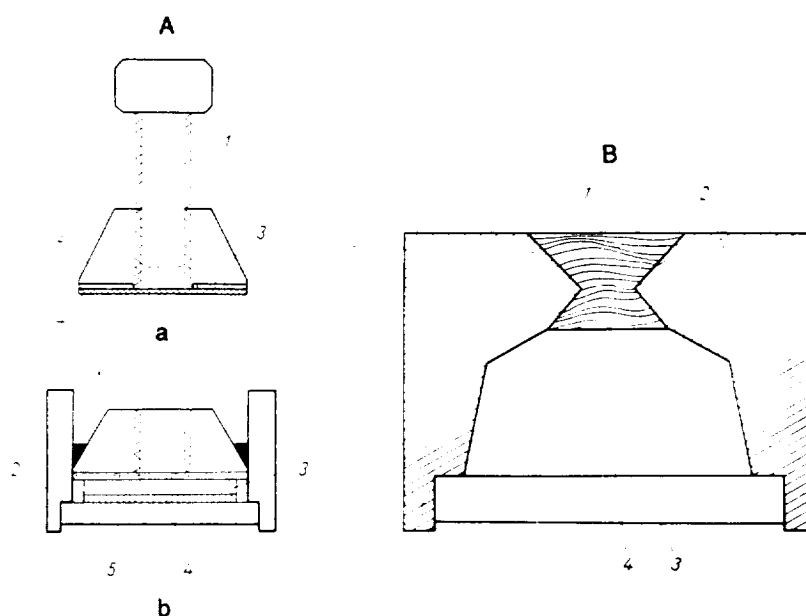


Figure 1: Cuvette design

A - dry yeast cells or fungi spores were housed in a monolayer on a microfilter for UV irradiation in space.

a - diagram of the mounting device; 1 - mounting bolt; 2 - lexan plug; 3 - adhesive layer; 4 - secondary filter

b - cross-section of cuvette: 1 - wax plug; 2 - wall of the cuvette; 3 - back filter; 4 - microfilter; 5 - quartz window.

B- yeast cells or fungi spores were housed in 0.05 ml water in a concentration that did not interfere with UV irradiation during exposure to space. The walls of the cuvette had a 7° slope to prevent shadowing of the cells. 1 - wax plug; 2 - wall; 3 - quartz window; 4 - cell suspension

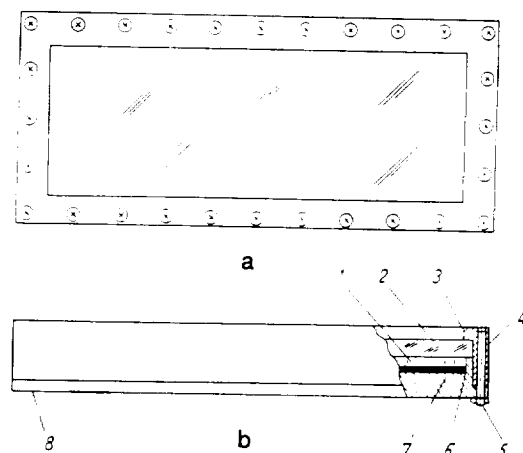


Figure 2: Microbial Ecology Evaluation Device for exposure of liquid cultures to the vacuum of space (temperature supported at $20 \pm 5^\circ$).

a - top view; b - side view; 1 - cuvette; 2 - quartz window; 3 - rubber cushion; 4 - cover; 5 - screw and nut; 6 - ring; 7 - rubber sponge; 8 - base.

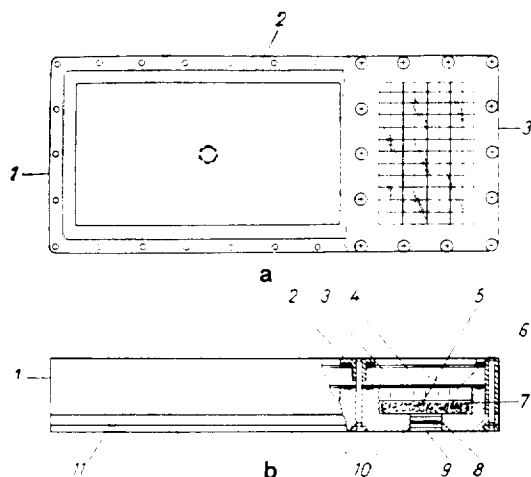


Figure 3: Microbial Ecology Evaluation Device with opening for equalizing pressure for exposure of cuvette to the vacuum of space

The device withstands impact acceleration of 78 G for 25 msec. There are two filters. The quartz bandpass filter has maximal transmittance at 254, 280, or 300 nm. The neutral density quartz filter attenuates solar radiation over a range of 4×10^1 - 8×10^8 erg/cm².

a- view from above: 1 - bottom, 2 - opening for equalizing pressure, 3 - cover, 4 - bolt; b - side view; 1 - cover; 2 - plug; 3 - filters; 4 - quartz window; 5 - rubber sponge, 6 - cuvette, 7 - sealing ring, 8 - filter with pores 0.2 μ in diameter; 9 - opening; 10 - pores 0.2 μ in diameter; 11 - mounting frame.

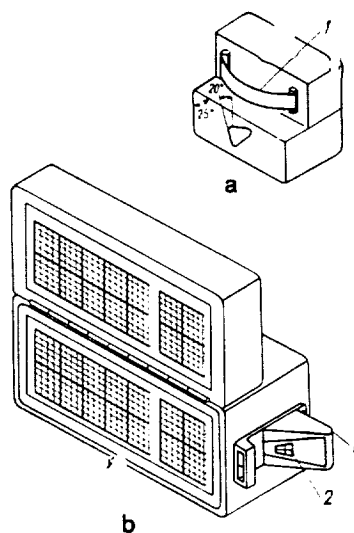


Figure 4: Microbial Ecology Evaluation Device deployed.
a - front view. 1 - handle; b - back view 1 - facing the sun, 2 - image location. One (control) cuvette remained in darkness in the lower compartment. The image was used for visual monitoring of the orientation of the device with respect to the Sun. An angle of 90° was maintained by computer-controlled maneuvering of the spacecraft

P1149(25/89)* Il'in VK.

Drug resistance of *E. coli* isolated from cosmonauts.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 90-91; 1989.

[9 references; none in English]

Microbiology, *E. coli*, Drug Resistance
Humans, Cosmonauts
Space Flight, Salyut-7

Abstract: Strains of coliform bacteria were isolated from the intestines of cosmonauts 7 days preflight and 2 days postflight. Cosmonauts involved were apparently members of Salyut-7 prime and visiting crews. The strains isolated were studied for sensitivity to broad spectrum antibiotics: tetracycline, chloramphenicol, streptomycin, kanamycin, neomycin, monomycin, ampicillin, disodium carbenicillin, polymixin, and gentamycin by determining the minimum inhibitory concentration. Conjugation was performed in liquid nutrient media using R-plasmid strains of *E. coli* C-600 as the recipient. Plasmids were studied by the method of electrophoresis in an agarized gel. A total of 450 strains of coliform bacteria were studied.

Most coliform bacteria from the intestine of one visiting crewmember were resistant to tetracycline, chloramphenicol, streptomycin, kanamycin, neomycin, monomycin, ampicillin, and disodium carbenicillin preflight. All determinants were transferred *in vitro* with frequency of $1 \cdot 10^{-4}$ - $2.5 \cdot 10^{-5}$. The plasmids isolated had molecular weight of 65 md. They were capable of spontaneous elimination, and various determinants of resistance were eliminated with varying frequency. This was an indirect proof that the plasmids were cointegrates from several plasmids. The determinant of resistance to tetracycline was very resistant and was not eliminated either spontaneously or in response to ethylidene bromide. This determinant was not transmitted in conjugation of the resistant strain of *E. coli* C-600; however, it could be mobilized for transfer by plasmid R, DRD₁₉.

Postflight, the majority of isolated coliform bacteria cultures from the prime crew were resistant to tetracycline. There had been no resistant strain preflight, suggesting that those found later had arisen through microbial and plasmid exchange with visiting crewmembers. The plasmids isolated from the resistant lines were nonconjugating (nontransmissible), suggesting that they were segregants of a polyresistant plasmid, possibly the one identified in the visiting crewmember. An electrophoretic analysis of a tetracycline resistant clone of this plasmid and one from the prime crewmember showed them to be identical. This demonstrates the possibility of exchange of resistant strains containing R-plasmids in space.

An analogous situation was examined in a 30-day simulation experiment, in which over the course of 7 days an analogous plasmid was disseminated among 4 subjects. This plasmid was eliminated in the course of 12 days. On day 19, it was no longer present in the strains in which it had been found previously. The eliminants retained only resistance to tetracycline. Electrophoresis suggested that the determinant of tetracycline resistance was represented by a transposon associated with the plasmid and inverted after its elimination in the chromosome. Restrictive analysis revealed common DNA fragments of the initial plasmid and transposon. It did not appear possible for this plasmid to return to its initial hosts, and it was most likely to enter the genome of some transient foreign strain. Indeed, in the simulation the plasmid was found on day 21 in lactose-negative hemolytic active strains of coliform bacteria that did not previously display drug resistance. Restrictive analysis showed the two plasmids to be

homologous. The author points out that the exact relationship between the determinant of resistance to antibiotics and pathogenesis had not been established for cosmonauts.

MUSCULOSKELETAL SYSTEM

PAPERS:

P1137(25/89)* Gol'dovskaya MD, Vnukova ZE, Shvets VN, Rodionova SS, Orlov OI, Kabitskaya OYe.

Response of bone tissue and osteoclast population to diphosphonates and Vitamin D₃ in rats undergoing hypokinesia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 47-50; 1989.

[16 references; 12 in English]

Musculoskeletal System, Bone Tissue, Osteoclasts

Rats

Hypokinesia, Diphosphonates; Nutrition, Vitamin D₃

Abstract: Previously it was established that oral administration of 1-hydroxyethylidene-1,1-diphosphonate (HEDP) in a dose of 9 mg/kg did not have an osteotropic effect under exposure to hypokinesia. However, another diphosphonate, hydroxydimethylaminopropylidene diphosphonic acid (HMAPDA), under these same conditions increased bone mass compared to controls. It has also been established that active metabolites of vitamin D₃ have an osteotropic effect. This study investigated whether vitamin D₃ altered the effect of diphosphonates when the two preparations were used in combination. A total of 144 Wistar rats were used as subjects. One group (hypokinesia model) was housed in immobilization cages for the 45 days of the experimental period. The second group was suspended from a special set-up in a head-down position (hypokinesia with head-down tilt); the third group served as a control. Each of the three main groups of subjects were divided into six subgroups. Subgroup 1 received no drugs; subgroup 2 received an oral dose of 20 mg/kg of HEDP daily throughout the experiment; subgroup 3 received HMAPDA in a dose of 0.5 mg/kg daily; subgroup 4 received a daily dose of 1.25 µg vitamin D₃; group 5 — HEDP combined with vitamin D₃; and subgroup 6 — HMAPDA and vitamin D₃. All subjects received a diet containing recommended amounts of calcium and phosphorus. After the 45-day period animals were sacrificed and bones removed from various portions of the skeleton: the tibia, iliac, sternum, and lumbar vertebra. Bone tissue was fixed, decalcified, and embedded in paraffin. Sections 5-7 µm thick were prepared and stained with hematoxylin, eosin, and toluidine blue. The state of bone tissue was evaluated histometrically. The volume density of spongy bone was measured in the metaphysis and the volume density of bone was measured in the primary spongiosa. An ocular micrometer was used for morphometry. The width of the epiphyseal growth ring was measured. Number of osteoclasts were counted in individual slides. The iliac bone was isolated in each rat and impressions were made on slides with β-oxybutyrate dehydrogenases used as a tag for identifying cell nuclei. Data were analyzed statistically.

When HMAPDA was administered to control rats, the mass of spongy bone in the tibia increased by more than a factor of 2, while it increased in the area with the highest metabolic rate (primary spongiosa zone) by approximately 30%. When this same drug was administered to rats undergoing hypokinesia, bone mass in the tibia remained at the same level as the control. The other diphosphonate, HEDP, when administered orally, did not induce any quantitative changes in bone tissue, either in control or experimental animals. This was the case even though the dose (20 mg/kg) was raised to more than twice that used in previous studies. Vitamin D alone did not have a prophylactic effect on tibia bones of animals undergoing hypokinesia. The combination of HEDP and vitamin D was also without effect. The osteotropic

effect of a combination of vitamin D with HMAPDA, was the same as the effect of the latter on the tibia. No effects on width of the epiphysial growth layer were noted in any condition. Significant effects of HMAPDA, alone or combined with vitamin D, were not noted in the bones of the trunk or pelvis.

Hypokinesia (both models) led to a decrease in the number of osteoclasts. This effect was not modulated by administration of any of the experimental substances. In the control (normal movement) condition, administration of HEDP increased number of osteoclasts, while administration of HMAPDA decreased them. Addition of vitamin D had no effect in either case. Both hypokinesia treatments decreased the number of osteoclasts with two nuclei, suggesting disrupted genesis of young cells. HEDP administered to control subjects and subjects exposed to hypokinesia (but not those undergoing head-down tilt) increased the number of osteoclasts with multiple (>2 nuclei). Administration of HMAPDA normalized all changes in distribution of cells with differing numbers of nuclei associated with hypokinesia. Effects of vitamin D on populations of osteoclasts were similar to those of HMAPDA. Addition of vitamin D to diphosphonates did not modulate the effects of the latter.

Table: Volume density of spongy bone in the metaphysis of the tibia

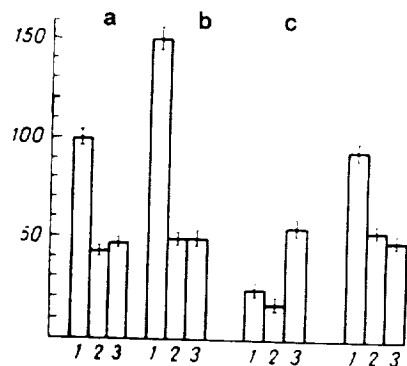


Figure 1: Change in total number of osteoclasts after exposure to hypokinesia alone (a) and hypokinesia plus HEDP (b), HMAPDA (c) and vitamin D₃ (d). Abscissa: - 1 control; 2 - hypokinesia; 3 - hypokinesia with head-down tilt; Ordinate - number of osteoclasts (in % compared to intact controls)

Figure 2: Distribution of osteoclasts with various numbers of nuclei in the total population of osteoclasts under exposure to hypokinesia alone (a) and combined with HEDP (b), HMAPDA (c), and vitamin D₃ (d)

P1159(25/89) Kozlova VG, Il'nitskiy VV, Dronenko SV.

Changes in the mechanical properties of muscles during a tilt test before and after immersion hypokinesia.

Voyenno-Meditsinskiy Zhurnal.

1989(4): 58.

[No references]

Musculoskeletal System, Muscles, Mechanical Properties

Humans, Athletes

Dry Immersion, Tilt Test

Abstract: Subjects in this experiment were 16 athletes (9 decathlon competitors and 7 gymnasts), aged 21-29. Subjects underwent "dry" immersion for 3 days.

Seismomyotonography was used to record frequency of muscle oscillation, which was taken as a parameter of muscle elasticity. Elasticity of the tibia, gastrocnemius, and head of the quadriceps of the femur was measured in the horizontal position, in minutes 1, 5, 10, and 15 of a tilt test and, in minutes 1, 5, and 10 after its termination.

Baseline measurements showed that participants in the decathlon displayed an increase in tibia muscle elasticity in response to the tilt test, while the parameter was virtually unchanged in other subjects. Gymnasts displayed elasticity increase in the the medial head of the gastrocnemius, as well as in the tibia. Changes after immersion in response to tilt were similar in nature, but the elasticity parameter was lower and the changes after tilt less pronounced than before treatment. Gymnasts showed less decrease in tolerance of the tilt test after immersion than decathlon athletes. The authors conjecture that these results may be due to differences in the muscles used by the two groups of athletes to regulate the position of their center of gravity.

P1167(25/89) Kuznetsov SL, Stepanov VV.

Response of striated skeletal muscle fiber in humans to long-term hypokinesia with head-down tilt.

Arkhir Anatomii, Gistologii, i Embriologii.

1989(7): 53-59.

[11 references; 6 in English]

Authors' affiliations: Institute of Biomedical Problems, USSR Ministry of Health; I. M. Sechenov First Medical Institute, Moscow.

Musculoskeletal System, Skeletal Muscle Fibers

Humans

Hypokinesia With Head-Down Tilt, Long-Term; Exercise

Abstract: Studies were conducted of biopsied skeletal muscle tissue of eight men who had undergone hypokinesia with head-down tilt (-6°) for a period of 360 days. Special exercises were performed in the head-down tilt position. Every 60 days the type and intensity of the exercise was changed. Group 1 ($n=3$) began the exercise program on day 21 of treatment. In their case the program included, during various periods: completely passive exercise (extension, use of vibrator); strength building exercise; and locomotor exercise. Exercise was highly strenuous, with the exception of the first 40 days. In group 2 ($n=5$) exercises were begun on day 121, and were not strenuous (with the exception of days 180-240 and 300-360). Exercises were performed either once or twice a day, for 60 or 120 minutes, respectively. Before treatment started and on days 120 and 360, needle biopsies were performed on the gastrocnemius muscle. Tissue obtained was frozen in liquid nitrogen. Cryostatic serial sections 10 μ thick were prepared. A portion of the material was fixed in 2.5% glutaraldehyde, again fixed in osmotic tetroxide, and embedded in araldite. Serial sections were examined for: activity of Ca-dependent ATPase myosin in a preincubated medium with pH of 4.3, and the two main types of muscle fibers slow (type I) and fast (type II) were identified. Activity of NADH-tetrazole reductase (NADH-TR), succinate dehydrogenase (SDH), and muscle lactate dehydrogenase (LDH) was measured using phenasinmetasulfate tetrazole methods. Concentrations of glycogen, RNA, and total protein were also evaluated using a scanning micrometer. Cross sectional area of the fibers was measured. Changes were expressed in percentage of baseline if absolute differences were significant at $p \leq 0.05$. Ratios between Type I and II fibers were computed.

Throughout almost the entire period of bedrest, no obvious morphological changes were observed in muscle tissue. Beginning on day 120, biopsied tissues from both group contained isolated fibers that, when stained using tetrazole methods, showed atypical clusters of granules of formazan in the center. After 360 days, local thickening began to be observed in the endo- and perimysia in both groups. Group I subjects showed clusters of fibers that were smaller than those surrounding them. Ratio between types of muscle fiber changed throughout the experiment.

Electron microscopy revealed that in group II both the contractile and the metabolic systems of the fibers had suffered considerably by day 120. A portion of the mitochondria was changed substantially: the matrix was homogenized, cristae were absent, the external membrane was fragmented. In myofibrils, threads of actin and myosin were arranged haphazardly and the Z-line was fragmented. Large areas of myofibril destruction were filled with fine-grained substance. In group I, ultrastructural changes were analogous on day 120, but less severe. After 360 days, myofibril destruction had progressed in group II, despite the exercise program. Threads of myosin and actin had disappeared, while the Z-lines had been partially retained,

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suggesting retention of the cytoskeleton, but destruction of the contractile system. Changes in group I were analogous but less severe.

Hypokinesia lasting 120 days primarily affected Type I fibers, which decreased in size. These results are consistent with animal space flight data, but differ from results obtained after 30 days of head-down tilt, in which both fiber types were affected. Diminished levels of RNA, total protein, and glycogen, and decreased activity of catabolic enzymes in both types of fibers testify to atrophy. The lack of correlation between changes in size of Type II fibers and concentration of protein suggests swelling of the fibers, possibly due to fluid redistribution. Physical exercise during 120-days of hypokinesia with head-down tilt impeded decrease in Type I fiber size and led to an increase in Type II fiber size. However, concentrations of RNA and total protein decreased (to a lesser degree than in group 2). Activity of ATPase and SDH did not differ from baseline, thus energy metabolism was maintained. LDH activity was depressed in both types of fibers. This may be considered a decrease in reserve capacity for energy production in these fibers in response to exercise. A significant decrease of glycogen in both fiber types in both groups suggests that this is a significant source of energy during hypokinesia and one which is not replenished.

On day 360 of treatment, group 2 subjects showed atrophy of muscle fibers (especially Type I) and significant decreases in metabolism. Group I showed some similar changes, but concentrations of total protein and glycogen remained normal in Type I fibers.

The authors conclude that increasing duration of hypokinesia increases atrophy of muscle fibers. The positive effects of exercise depend on how much restructuring they have already undergone: the more they have suffered, the less likely they are to be restored. Commencement of exercise in the earlier hypokinesia period and greater exercise intensity are recommended. The retention of the cytoskeleton of muscle fibers while threads of actin and myosin are destroyed may provide a structural basis for further recovery of muscle fibers during readaptation.

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Table : Changes in Type I and II muscle fibers in response to hypokinesia with head-down tilt and this treatment combined with exercise at different points in the experiment (in % of baseline)

Parameter	120 days			
	Group 1		Group 2	
	Type 1	Type 2	Type 1	Type 2
Cross section area	80.5±5.7	93.7±13.6	95.3±8.9	144.1±5.3
Concentration of RNA	63.1±4.2	74.6±3.1	82.9±3.3	72.0±3.9
Total protein concen.	79.4±5.4	75.4±3.1	94.1±3.2	89.8±4.3
NADH-TR activity	37.6±3.1	82.4±3.6	101.4±8.3	90.9±11.3
SDH activity	61.9±3.1	98.1±4.3	91.2±10.5	105.7±11.2
Glycogen concen.	58.5±10.1	36.5±11.2	42.7±9.9	54.2±10.1

Parameter	360 days			
	Group 1		Group 2	
	Type 1	Type 2	Type 1	Type 2
Cross section area	53.1±10.1	71.9±4.5	92.1±17.1	84.9±3.7
Concentration of RNA	54.7±6.2	59.7±7.1	87.4±2.9	74.1±2.8
Total protein concen.	64.6±6.8	67.1±5.9	100.7±9.2	97.3±8.1
NADH-TR activity	47.7±5.1	42.9±4.9	82.1±3.8	95.8±5.9
SDH activity	82.3±3.8	85.5±2.9	64.4±3.7	84.0±4.3
Glycogen concen.	83.7±4.2	80.2±3.9	102.3±5.1	95.6±7.2

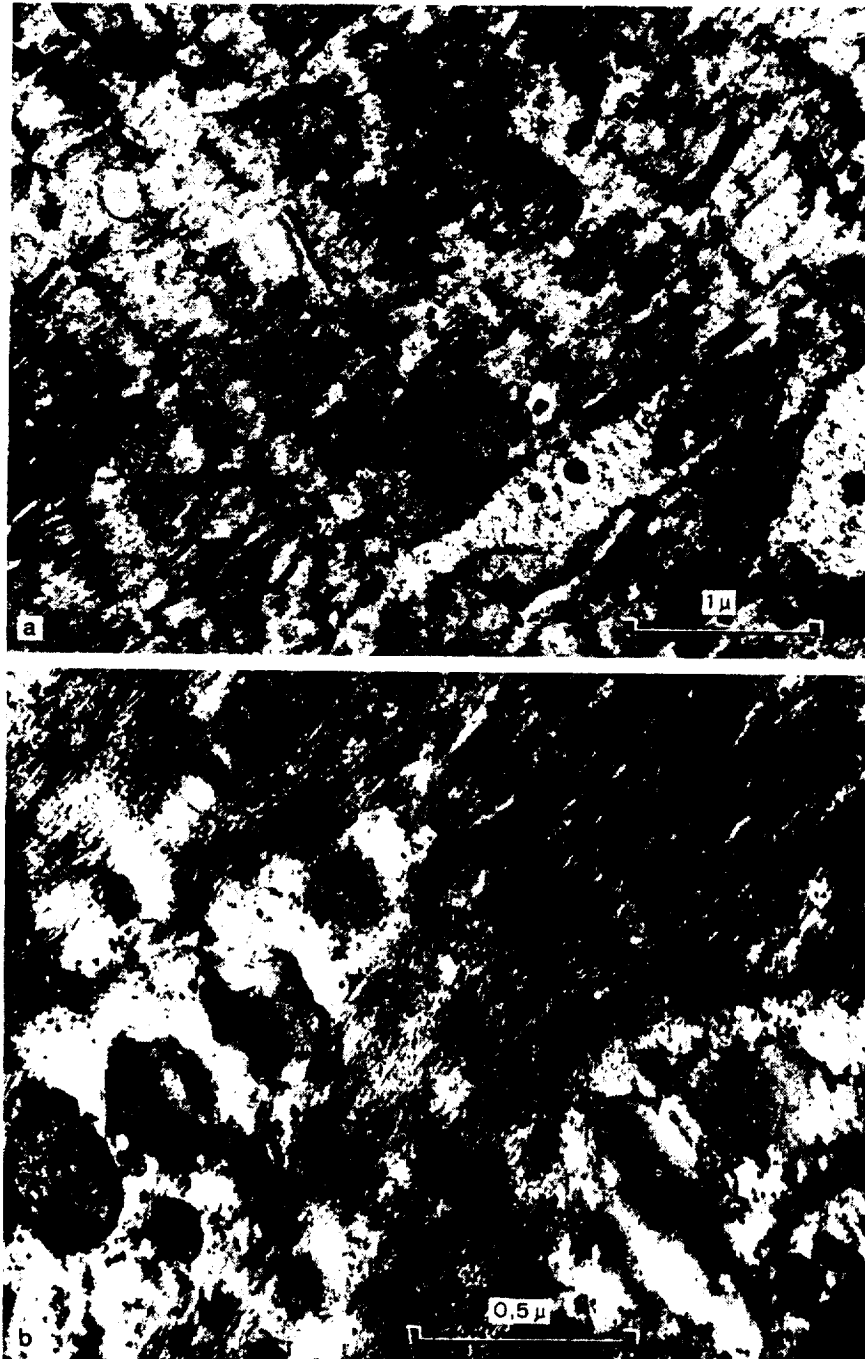


Figure 1: Changes in human skeletal muscle fibers in response to hypokinesia with head-down tilt on day 120 of treatment

a - hypokinesia only; b - hypokinesia + exercise

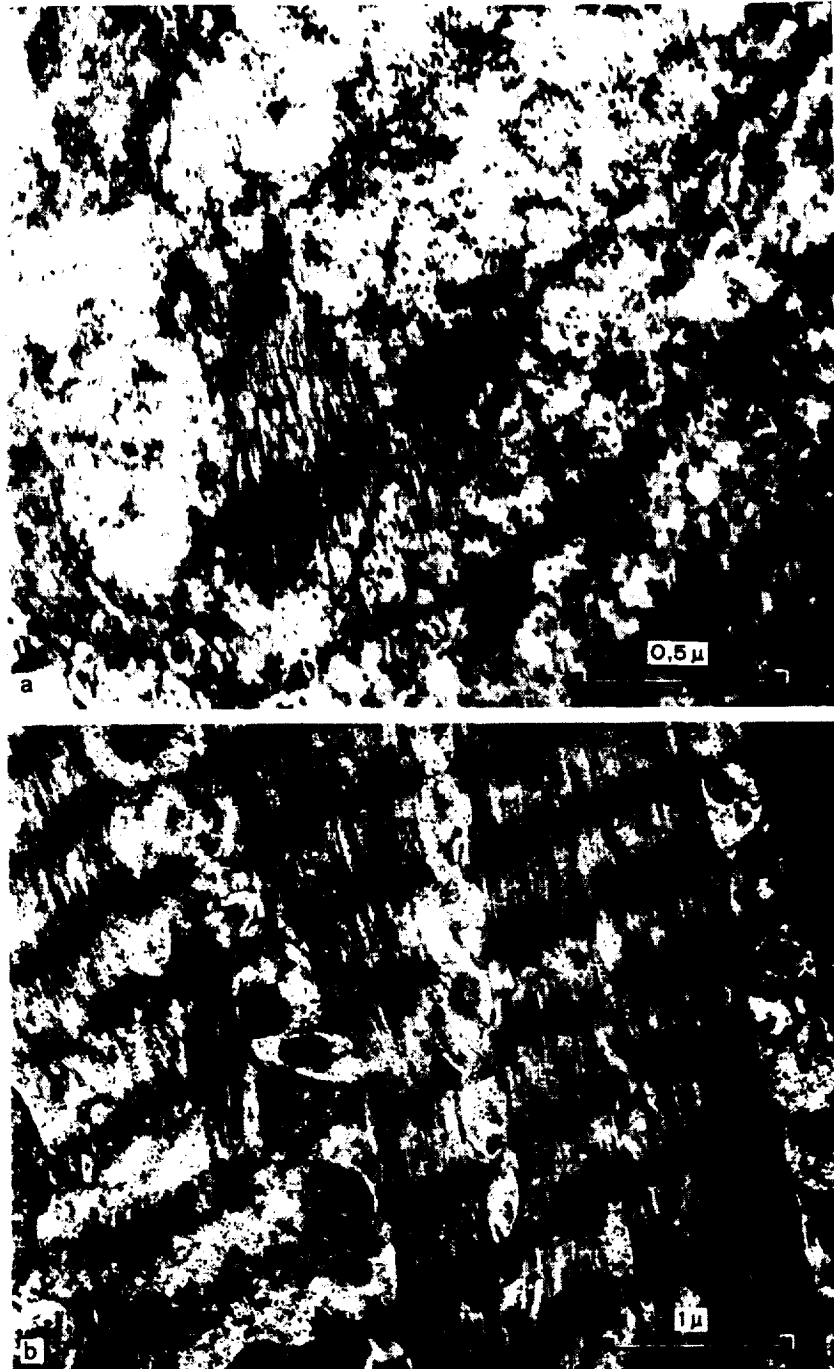


Figure 2: Changes in human skeletal muscle fibers in response to hypokinesia with head-down tilt on day 360 of treatment

a - hypokinesia only; b - hypokinesia + exercise

MONOGRAPH:

M151(25/89) Stupakov GP, Volozhin AI.

Kostnaya Sistema i Nevesomost'; Костная Система и Невесомость

The Skeletal System and Weightlessness.

Moscow: Nauka; 1989.

Problemy Kosmicheskoy Biologii, Tom 64, Проблемы Космической Биологии; Том 64 (Problems of Space Biology. Volume 64)

Note this is a translation of an announcement published in a journal; we currently have no additional information about this monograph.

KEY WORDS: Musculoskeletal System, Bones, Humans, Cosmonauts; Rats, Tortoises, Dogs, Primates, Space Flight, Long-Term, Weightlessness

Announcement: This book cites data concerning changes in bones in cosmonauts during long-term space flights. It considers the potential pathogenetic mechanisms of gravity-induced changes in the weightbearing skeleton. A great deal of attention is devoted to methods for investigating mineralized tissue: biochemical, pathomorphological, mechanical and others. The authors use results of experiments performed on rats, tortoises, dogs, and primates as the basis for describing changes in various portions of the skeleton and extent of recovery. They cite data on the effects of gravitational unloading on the physical and mechanical properties of bone. They analyze the effectiveness of methods for correcting and preventing changes in bone due to weightlessness and hypokinesia.

NEUROPHYSIOLOGY

P1130(25/89)*Ponomarenko VA, Yegorov SV, Zhernakov OV.

Potential use of evoked potential of the brain in diagnosis of fatigue in flight personnel.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 21-23; 1989.

[20 references; 9 in English]

Human Performance, Fatigue

Humans, Flight Personnel

Neurophysiology, Evoked Brain Potential, Diagnosis

Abstract: A pilot training simulator was used to model a 10-hour flight with alternating cycles of automatic and manual control. Before and after this task, subjects performed two landing approach tasks. Subjects were four apparently healthy individuals who had mastered the use of the training simulator. A total of seven sessions were run. A monopolar electroencephalogram was recorded while the subjects performed the landing approach task. Irrelevant acoustic stimuli (clicks) were used to obtain evoked potentials. Interstimulus intervals were 7 seconds. EEG records were averaged using a minicomputer. Parameters considered included latencies and amplitudes of identified EEG components. Subjects rated their sensations of fatigue before and after the experiment. Performance was evaluated on the basis of speed and accuracy in the landing task.

Acoustic evoked potentials were obtained for all subjects. Potential configuration tended to be stable for each individual throughout the experiment. Visual analysis of the acoustic evoked potentials showed that the most prominent components were the N₁ and P₂ waves with latent periods of approximately 90 and 175 msec, respectively. For this reason the N₁P₂ peak-to-peak amplitude was selected as the major parameter for study. While subjects performed the landing task, N₁P₂ amplitude decreased by 28.3% compared to the analogous value at rest. After performance of the 10-hour simulated flight, performance on the landing task decreased significantly. N₁P₂ amplitude also decreased over this period (by a mean of 24.5%), but no other regular changes in evoked potential were noted.

Figure: Change in parameters of performance and N₁P₂ amplitude of acoustic evoked potential while performing a landing approach task before and after a 10-hour simulated flight

P1131(25/89)* Petrenko YeT.

Work capacity and spatial-temporal organization of brain biopotentials of operators

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 23-26;1989.

[14 references; 3 in English]

Human Performance, Work Capacity, Interference Resistance

Humans, Operators

Neurophysiology, Brain Biopotentials

Abstract: This study investigated the effects of light stimuli with frequency of 12 Hz on productivity of performance on a complex operator task and inferred information about processes of intercentral integration of the functional systems of the neocortex on the basis of the spatial-temporal organization of biopotentials. A total of 18 individuals, aged 18-28, participated as subjects. The operator task was a complex electronic game using a microcomputer, played under time pressure and requiring intense concentration, rapid information processing and visual-motor response, and accuracy. Game score was computed automatically. While subjects were playing, EEGs were recorded from frontal, lower parietal, visual areas, and the motor areas for the hand muscles in both hemispheres. Five-second segments of the EEG were analyzed.

Light interference (evidently flashes at 12 Hz) led to a reliable decrease in task performance, amounting to 36% compared to normal conditions. During task performance under normal conditions, the spectrogram of the frontal, motor and lower parietal brain areas showed a prominent peak in the 68 Hz band and a high degree of coherence of these frequencies. With light interference of 12 Hz, the density of the EEG wave corresponding to the flash frequency (12 Hz) increased significantly. The greatest increase in these frequencies (152%) was noted in the left motor area and the least in the left frontal area. Interference also significantly decreased the spectral density of the EEG waves in the 6-8 Hz band. There was a significant decrease in the coherence of biopotentials at these frequencies between the left frontal region and the motor representation of the muscles of the right hand, and between the left lower parietal region and the motor centers of the right hand. Cross-spectra and coherence functions of symmetrical motor areas in both hemispheres underwent significant changes. Interhemisphere coherence was considerably less affected in the frontal areas.

The author concludes that decreased effectiveness of operator performance in response to flashing lights is evidently due to disruption of functional interactions among neural centers responsible for psychomotor activity. The most important phenomenon is the disruption of spatial-temporal synchronization of biopotentials at frequencies of 6-8 Hz. However, the brain (particularly the frontal areas) showed significant resistance to exogenous synchronization at the frequency of the light flashes, and this is assumed to account for the relative resistance of psychomotor performance to interference.

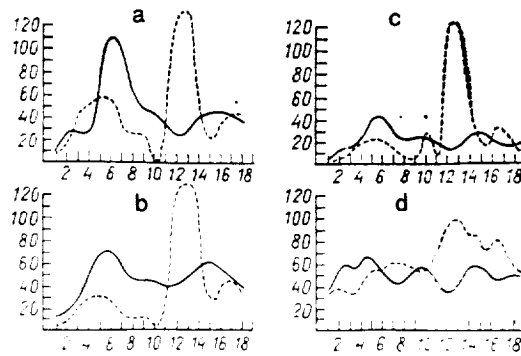


Figure: Autospectrogram of the left frontal lobe (a), motor representation of the muscles of the right hand (b), their cross spectrum (c), and coherence functions (d) of subject S. during operator performance under normal conditions (solid line) and during exposure to flashing light at 12 Hz (dotted line)

P1140(25/89)* Repin AA.

Characteristics of visual-vestibulomotor interactions in experimentally induced labyrinth asymmetry.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 59-64; 1989.

[26 references; 16 in English]

Neurophysiology, Visual-Vestibular Interaction

Humans

Labyrinth Asymmetry

Abstract: This work compared changes in coordination of eye and head movements in two gaze fixation paradigms (trigger and predictive) after labyrinth asymmetry was experimentally induced through electrical stimulation. Subjects were 16 men and 3 women with no history of relevant pathology. Subjects were seated in front of a white curved screen 60 cm in diameter. Light targets subtending a visual angle of 1° were located at distances 20, 40, and 60° to either side of center. In the trigger paradigm, peripheral visual targets were presented with no warning in random order subsequent to central fixation. Predictive fixation was studied when the gaze was transferred from peripheral to central fixation. The task involved rapid and accurate fixation of the targets. Eye movements were analyzed using electro-oculography with electrodes attached to the skin in the area of the lateral corners of the eyes. Head movements were recorded through potentiometry with the subjects wearing a helmet. Displacement of the gaze from the central position and back again was measured by graphic summation of the curves of eye and head movement. Threshold of excitation of the labyrinth was considered to be the level of excitation causing deviation of the eyes by $4-6^\circ$ from initial position. The exciting electrode was placed in the area of the tragus, and the indifferent electrode was attached to the right palm. Stimulation was monopolar and monaural and no less than 100 msec. in duration. Initial current of 0.44 mA did not induce movements of the head or eyes. Stimulation was repeated at intervals of no less than 5 seconds and the entire session lasted 10 minutes or more.

Gaze fixation triggered by the sudden appearance of a light on the periphery of the visual field gave rise to rather rapid and accurate gaze fixation. The fixation response had three components: a saccad, head turning, and compensatory eye movement subsequent to the saccad and during the head-turning response. In 30% of the cases, there was an error of $3-5^\circ$ which was corrected by a second saccad. Fixation in the predictive paradigm had four components: head turning in the direction of the target; compensatory movement of the eye in the opposite direction; a saccad in the direction of the target; and a second compensatory movement, opposite in direction to the head turning. There were no positional errors in this paradigm, so secondary compensations were not needed. Threshold monopolar monolateral stimulation of the labyrinth evoked a two-phase oculographic response, involving a phasic ipsilateral deviation of the eyes followed by a tonic contralateral deviation. In the trigger paradigm, rates of compensatory movements were slowed, increasing the time required for gaze fixation. There was some asymmetry between movements to the right and left, but the difference was not significant. Magnitude of positional errors increased. When stimulation was above threshold, changes were more pronounced, including decrease in rate of saccad, with ipsilateral saccads increasing in amplitude and contralateral saccads decreasing. Changes in head turning were insignificant, but there was a marked divergence in rates of compensatory eye movements with rate of contralateral movements decreasing and of ipsilateral movements increasing. Time required for fixation increased to 60-80% above baseline. In the predictive paradigm, threshold stimulation led to increase in the head movement rate and amplitude parameters of head movement, with virtually unchanged contralateral movements. The ratios between maximal

rates of eye and head movements in phases 1 and 3 were altered. The authors concluded that unilateral stimulation of the labyrinths evokes disruption of coordination of head and eye movements in both fixation paradigms.

Table 1: Major parameters of components of gaze fixation in the trigger paradigm under normal conditions and labyrinth asymmetry evoked by threshold and superthreshold stimulation with electric current

Table 2: Major parameters of components of gaze fixation in the predictive paradigm under normal conditions and labyrinth asymmetry evoked by threshold and superthreshold stimulation with electric current

Figure 1: Coordination of eye and head movements in the trigger and predictive fixation paradigms in healthy subjects in response to presentation of a target 40° from center

Figure 2: Threshold of two-component eye movement response to monopolar left stimulation of the labyrinth with electric current with duration of 100 msec and power of 1 mA

Figure 3: Coordination of eye and head movements in the trigger paradigm of fixation for a target 40° to the right of center during right and left stimulation of the labyrinths with an electric current

P1141(25/89)* Shumilina VF, Preobrazhenskiy NN.

Study of the otolith membrane of the sacculus and utricle of a guinea pig.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 64-69; 1989.

[45 references; 39 in English]

Neurophysiology, Otolith Membrane, Otoconia
Guinea Pig
Anatomical Study

Abstract: This paper describes the results of a detailed study of the otoconia of the otolith membrane in the sacculus and utricle of adult guinea pigs. A scanning electron microscope was used. Animals were anesthetized and the otolith membrane isolated and fixed. The tissue was dehydrated and dried. Samples were mounted on metal, and coated with palladium and scanned.

Two types of otoconia were found — normal and those with altered geometric form and/or wrinkled surfaces. They occurred on both the utricle and sacculus, but were more common and more complex on the latter. Typical of the utricle were otoconia with smooth surfaces but differing proportions than normal ones. The sacculus contained more otoconia that were similar in shape to normal ones but displayed various changes of the surface. Conglomerates of normal otoconia were also found.

Figure 1: Scanning electron microscopy. Normal otoconia of guinea pigs in the utricle and sacculus of the otolith membrane

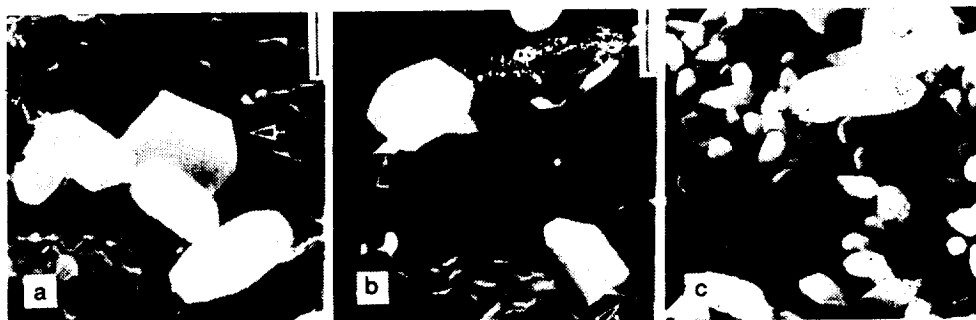


Figure 2: Scanning electron microscopy. Abnormally shaped otoconia in the utricular otolith membrane of guinea pigs.

a, b, otoconia with smooth surface; b - truncated otoconia with flat tops; c - giantotoconia in the area of the striole? with coarse-grained surface and marked scaly excrescences. Scale: 5 μm (a,b) and 10 μm (c)

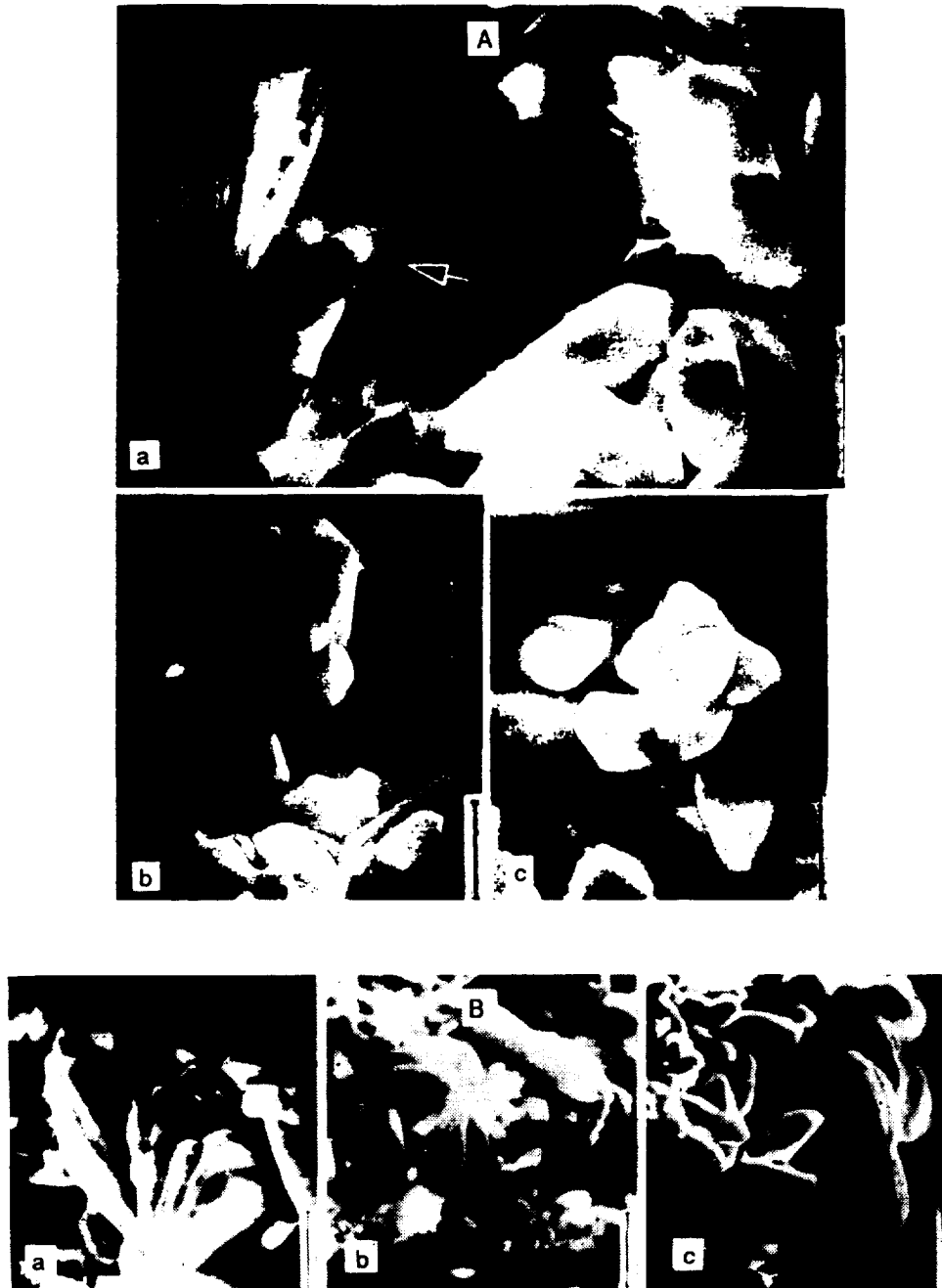


Figure 3: Scanning electron microscopy. Abnormally shaped otoconia of the saccular otolith membrane of guinea pigs.

A - conglomerate otoconia, forming from normal otoconia with smooth surfaces: a - joining at lateral surface along the longitudinal axis (arrow); b, c - growing together at the lower end surfaces; B - conglomerate otoconia forming from abnormally shaped otoconia with coarse-grained surface: a, b - rosettes; c - bundle. Scale: 5 μ m

P1158(25/89) Ivanov AB.

Change in reflexive vestibular activity in response to upright position.

Vestnik Otorinolaringologii.

1989(4): 16-19.

[15 references; none in English]

Author's affiliation: Laboratory of Clinical Otoneurology, Belorussian Scientific Research Institute of Neurology, Neurosurgery, and Physiotherapy, Minsk

Neurophysiology, Vestibular Activity, Reflexive, Nystagmus

Humans, Males

Tilt Tests, Stand Tests

Abstract: This paper describes a study of vestibular excitability in 19 healthy males, aged 18-33, during stand and tilt tests. Vestibular stimulation involved monothermal caloric irrigation with water at 25°C. Response was recorded by electronystagmography. The traditional parameters of reflexive nystagmus were measured: latent period, number of oscillations, frequency and duration of nystagmus, amplitude and rate of the slow phase. The effect of upright position was evaluated on the basis of maximal changes in parameters of vestibular nystagmus as the subject moved from supine to standing position. Both active (stand) and passive (tilt) orthostatic tests were used. Measurements were made in baseline as well as upright position.

In the stand test, all parameters of reflex nystagmus, except for latent period and frequency, showed a tendency to decrease. In almost all subjects, latency increased significantly, increases in frequency were not statistically significant. All decreases were statistically significant. These results are interpreted as demonstrating decreased reactivity of the vestibular system.

When a passive tilt test was performed on three subjects, all nystagmic parameters, with the exception of latency, decreased considerably more than in the active stand test. Since the hemodynamic factor would have been similar in both studies, the author concludes that the major factor was the effects of somatic afferentiation on vestibular centers of the brain stem. This shows that the neurophysiological nature of the effects of somatic afferentiation on nystagmic activity is very complex. In the first experiment the activation of postural reflexes led to a partial depression of the reaction, while in the second experiment the virtually complete elimination of proprioceptive reflexes led to strong inhibition of the reactivity of the vestibular system.

Table 1: Change in the major parameters of reflexive nystagmus in response to stimulation of the right labyrinth during a stand test

Table 2: Change in the major parameters of reflexive nystagmus in response to stimulation of the right labyrinth during a tilt test

P1165(25/89) Stoyanov AP, Netudykhatka OYu, Alekseyev SV, Grigro'yan RA, Rozanov VA, Yevstafyev VN.

Concentrations of GABA and glutamic acid in the brains of rats exposed to noise and vibration under conditions of a sea voyage.

Fiziologicheskiy Zhurnal.

35(2): 13-18; 1989.

[11 references; none in English]

Authors' Affiliation: Scientific Research Institute for Industrial Hygiene in Maritime Transport, Odessa

Neurophysiology, Brain, GABA, Glutamic Acid; Psychology, Conditioned Response

Rats, Males

Habitability and Environment Effects, Noise, Vibration

Abstract: Experiments were performed on 60 male Wistar rats, divided into three groups. The first group was housed in the engine room of a vessel and subjected to the highest level of noise (110 dB) and vibration (84 dB). The second group (ship control) was exposed to factors typical of crew living quarters with 60 db noise and 62 db vibration. The third group was housed on shore (shore control). Groups housed on the ship were protected from other adverse factors, such as temperature extremes. Animals had free access to food and water. A conditioned avoidance response was developed on days 7-10 and 30-35 of a 35-day transmeridial cruise. The conditional stimulus, a sound, was followed after 5 seconds by an electric shock through the grid floor of the box. When the conditioned response had been developed, the animals were decapitated and the brain removed; the cerebellum, brain stem, and cerebral cortex were isolated. These structures were homogenized and conserved in 96% ethanol. Free GABA and glutamic acid were measured in samples by a spirit-water extraction technique, followed by paper chromatography. Conditioned response latency in the avoidance task was recorded.

On day 7 both groups of animals exposed to ship noise and vibration showed an increase in avoidance response latency. Concentrations of glutamic acid and GABA were depressed in all areas of the brain studied to an almost equal extent for the two experimental groups. Effects on conditioned reflexes were more pronounced in rats exposed to the higher levels of noise and vibration. On day 35, avoidance response latency decreased (improved) in animals exposed to the higher level of noise and vibration compared to the first experimental stages; this parameter increased (worsened) for the group exposed to the lower levels of these factors. While glutamic acid in the brain did not change significantly in either group, compared to days 7-10, GABA increased in all portions of the brain in both groups to a level no different than that of the shore control group. Ratio of glutamic acid to GABA was inversely correlated with latency of avoidance response. Both increased GABA in the brain and increased latency are attributed to "activation of inhibitory processes," which is postulated to occur during the "resistance" stage of adaptation.

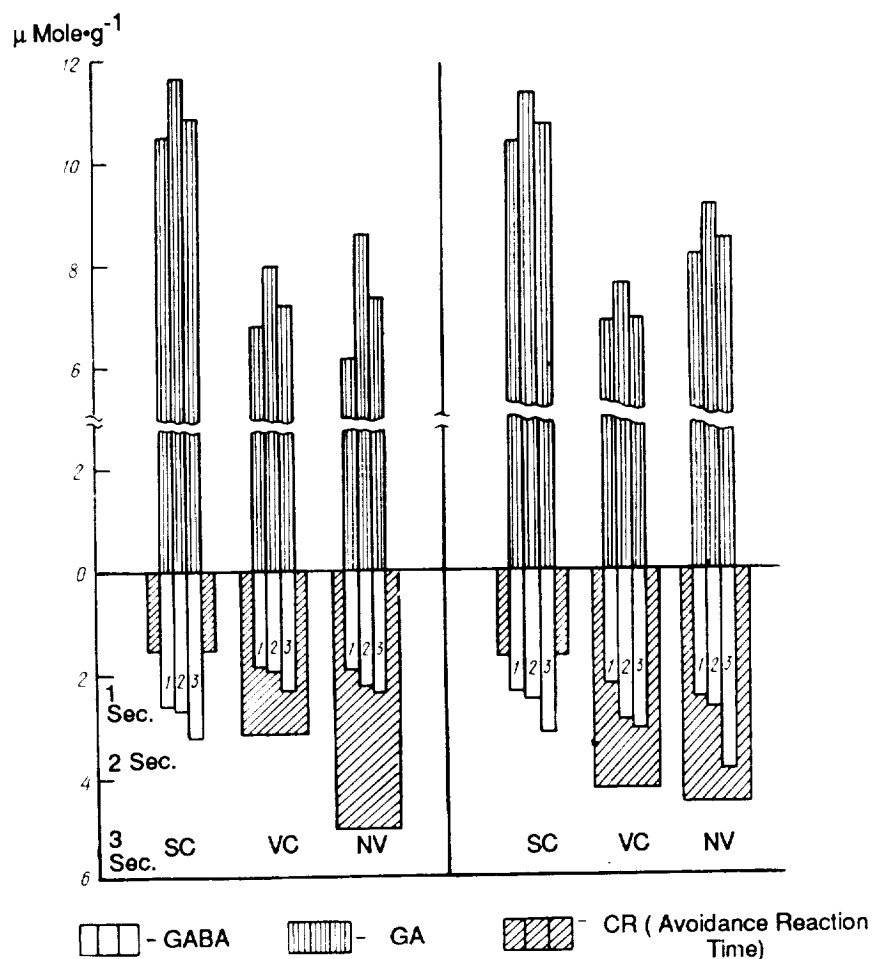


Figure: Changes in conditioned reflex performance, concentration of GABA and glutamic acids in the cerebellum (1), cerebral cortex (2), and brain stem (3) of the brain during a sea voyage with intense noise and vibration;

a -stage 1 of the experiment - 7-10 days; b - stage 2 - 30-35 days (SC - shore control; VC - vessel control; NV - noise and vibration)

NUTRITION

PAPER:

P1128(25/89)* Bychkov VP, Kalandarov S, Agureyev AN, Popov IG, Kochetkova AN, Ushakov AS.

Crew nutrition on Salyut-7.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 9-14; 1989.

[20 references; 9 in English]

Nutrition, Nutritional Status, Crew Rations; Menu Selection System

Humans, Cosmonauts, Prime Crews

Space Flight, Long-Term, Salyut-7; Flight Simulations; Isolation

Abstract: This paper discusses results of evaluation of the diet of Salyut-7 prime crews on flights 211, 150, 237, 165, and 126 days in duration and also of the use of cosmonaut rations on the ground under normal conditions and in simulation of individual flight factors. Preliminary testing of the rations was performed over a 68-day period with 5 healthy male volunteers as subjects. Conditions associated with testing were either normal or isolation in an airtight chamber with an atmosphere containing elevated ammonia. Salyut-7 was the first flight to utilize a new type of system for organizing the storage and selection of rations — the "menu-selection" system. Portions of the same menu item were stored together in containers instead of packaging all the components of each day's meal together. An inventory system in which each type of product, e.g. bacon, had an identifying number, and each portion provided also had a unique number, making it possible to readily determine what foods the crews were actually eating. To determine the adequacy of the diet, parameters of protein, lipid, carbohydrate, vitamin, and fluid-electrolyte metabolism were measured, as were the functional status of the adrenal gland, activity of a number of enzymes, and immunological reactivity and intestinal microflora. Total protein and its fraction, total lipids, total cholesterol, α -cholesterol, lipoprotein fractions, 11-oxycorticoid, alanine- and aspartate aminotransferases were measured in blood serum. Nitrogen, urea, ammonia, uric acid, creatinine, 17-ketosteroid, adrenalin, noradrenalin, of vitamins B₁, B₆ and C were measured in daily urine. In addition, N, Ca, P, K, Mg, and Na were measured in samples of rations, feces, and urine to measure their assimilation. The above studies were performed in cosmonauts pre- and postflight. Inflight studies were much more limited and included tracking of weight changes, and general physiological and clinical parameters. Amount of ration eaten was monitored. The rations were rated on a five-point scale for taste.

During the preliminary 68-day testing of the rations, all 5 subjects retained their appetites and evaluated ration taste as good (4-5 on a 5 point scale) and quantity as satisfactory. Digestive upsets were absent and body weights remained virtually unaltered. Assimilability was high and nitrogen balance was maintained. All other parameters remained within normal limits when living conditions were normal. Under conditions of isolation in an airtight chamber (6 days) and elevated atmospheric ammonia (37 days) the following changes were noted: decreased cholesterol, and proportion of α -cholesterol and α -lipoprotein; decreased renal excretion of thiamine and increased ascorbic acid; and activation of adrenal cortex functioning. In addition, there was a decrease in renal excretion of nitrogen attributed to decreased assimilation of protein, and a decrease in T-lymphocytes. Changes in intestinal microflora were noted. Introduction of increased ammonia did not cause any further significant changes in parameters compared to residence in the airtight chamber alone. Changes did not exceed the boundaries of the norm and returned to baseline during the recovery period.

NUTRITION

Study of cosmonauts' nutritional status during five long-term flights on Salyut-7 showed that the rations supported adequate health and performance. Cosmonauts showed no symptoms of dyspepsia and digestion was regular. Some products were criticized for taste and were replaced where possible. Most cosmonauts suffered only slight weight loss (mean 3.5 kg), but two lost 8.4 and 9.6 kg, which is attributed to inadequate use of prophylactic countermeasures. Ten of 12 cosmonauts maintained nutritional status close to baseline. As part of their training, cosmonauts ate nothing but cosmonaut rations for 12 days preflight, to reveal allergies and provide data on individual taste. Due to the way food products were stored, assembling the products a cosmonaut had selected for his meal was difficult and time-consuming for him. The authors suggest a return to the earlier "daily meal" system until product selection can be automated within the "menu-selection" system. The most frequent deviation from the diet stipulated during the Salyut-7 flight was a switch from a 4- to 3-meal system, which was typically associated with lack of time during a work shift. Extra time for work was obtained by sacrificing number of meals and their duration. The care with which products were selected to accord with the recommended diet also diminished somewhat.

The authors draw the following conclusions with regard to the nutritional system on Salyut-7:

1. All components of the system worked and were positively evaluated by the crew.
2. The diet consumed supported an adequate level of performance capacity and health for performance of the flight mission.
3. The system for obtaining information about what each crewmember eats during the flight needs improvement to allow ongoing evaluation of changes in nutritional status and provision of expert corrective recommendations if needed.
4. The menu selection system requires improvement, especially automation of the most time consuming processes.

Table 1: Metabolic parameters in preliminary subjects

Table 2: Body weight of crewmembers of Salyut-7 pre- and postflight

Crew	Crew-member	"Ideal"	Body weight, kg		
			Preflight	Postflight	Difference
First	1	65.9	66.0	61.5	-4.5
	2	71.8	78.0	69.6	-8.4
Second	1	66.4	79.0	75.5	-3.6
	2	74.1	72.0	66.3	-5.7
Three	1	63.2	73.5	74.8	+1.3
	2	78.2	76.5	73.5	-3.0
	3	66.4	72.0	62.4	-9.6
Fourth	1	74.6	77.0	78.4	+1.5
	2	75.1	72.0	71.4	-0.6
	3	73.6	74.5	71.2	-3.3
Fifth	1	63.6	75.0	74.5	-0.5
	2	79.1	76.1	71.5	-4.6

Figure: Mean daily nitrogen balance in subjects on a diet of cosmonaut rations

OPERATIONAL MEDICINE

P1142(25/89)* Khomullo GV, Lotova VI, Chernyayev AN.

The effect of somatropin on healing of skin wounds under conditions of hypoxia.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 69-73; 1989.

[18 references; 6 in English]

Operational Medicine, Wound Healing

Rats

Hypoxia, Somatotrophin

Abstract: Experiments were performed on 120 white male rats. Under anaesthesia, a surgical wound 225 mm² in area was made through all layers of skin on the left side of the body. Forty rats served as controls and received no further treatment; the remaining rats were exposed to hypoxic hypoxia by raising them to a height equivalent of 8200-8500 m in a barochamber daily for 8-10 hours. A portion (n=40) of these were injected intramuscularly with human somatotrophin (STH) twice a day in a dose of 2 mg/100 g. Injections began 1 day before the traumas and continued for the term of the experiment — 15 days. During the healing process, the area of the open wound was measured and recorded daily; cytological composition of tissue smears taken from the wound was studied 6, 12, and 24 hours after the operation; and the edges of the wound were biopsied 5, 10, and 15 days after the trauma. Activity of a number of enzymes was measured histochemically in the regenerating structures. These enzymes included succinate dehydrogenase (SDH), and acid and alkaline phosphatase. Rate of proliferation of epithelial and connective tissue cells was evaluated on the basis of inclusion of thymidine marked with tritium in the nuclei of cells of granulated tissue and epidermis bordering on the wound.

Results indicated a depression of the inflammatory reaction in animals exposed to hypoxia, as evidenced by decreased migration of neutrophils and agranulocytes into the wounded area, slowed transformation of relatively undifferentiated forms into polyblasts and macrophages, and decrease of cells of histogenic origin. A significant number of cells were subject to early destruction in the form of pyknosis, fragmentation, and lysis of the nuclei of neutrophils. The macrophages displayed degenerative vacuolization of cytoplasm and nuclear substance. Increased microbial contamination was noted in wounds of hypoxic animals. The fibroblast process was also inhibited under conditions of hypoxia. Granulation was uneven in the edges of the wound and there was pronounced destruction of cells, disruption of collagen formation and swelling and disintegration of collagen fibers. As a compensation, there was enhanced development of the capillary net. Epithelial regenerate was of poor quality. Activity of STH was depressed relative to control, suggesting disruption of redox reactions and attenuation of regeneration. Inhibition of proliferation in hypoxia was confirmed by the tracer study, appearance of the first labelled mitoses in the epithelium occurred only after 6 hours, compared to 3 hours in the control. At the end of the 15 day period the area of the open wound for the hypoxic group was 46.0 mm², while it had completely closed in 13 days in the control.

Use of STH in rats undergoing hypoxia activated all stages of the recovery process in the skin. Changes (compared to hypoxia alone) included acceleration of migration and increase in all cells in the exudate, active phagocytosis of microorganisms, and decreased signs of cell destruction. Epithelia regeneration was normal. Inclusion of ³H-thymidine was accelerated. On day 15, size of the open wound was considerably less than that in rats not receiving STH and exposed to hypoxia.

Table 1: Quantity of cells in the wound exudate in the animals

Table 2: Index of tagged nuclei in epithelial and connective tissue cells of various zones of regeneration

Figure: Young connective tissue in the area of the wound 15 days after the operation

SPACE BIOLOGY AND MEDICINE

P1151(25/89)* Voloshin VG, Naryshkin IYe, Yuganov YeM.

Some principles for evaluating the quality of scientific research and the extent of implementation of their results.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 94-96; 1989.

[4 references; none in English]

Space Biology and Medicine, Research and Implementation

Theoretical Article

Research Evaluation

Abstract: In this letter to the editor, the authors propose a system for evaluating research projects. A number is assigned to each project based on four factors, each of which is composed of rated values up to a stipulated maximum for a number of subfactors, with a weighting coefficient for each subfactor. The four factors and specimen subfactors are: 1) Methodology of the scientific research project and its appropriateness to the technical specifications. Sample subfactors: appropriateness of the methods selected, and their correspondence to the international state of the art; depth of analysis of results obtained, i.e., are conclusions and recommendations justified? Maximum point value 5. 2) Significance of results obtained. Sample subfactors: are results patentable?; How do they compare to the most advanced discoveries of Soviet and international science? Maximum point value: 5. 3) Quality of ultimate scientific product and extent to which it is implemented: Sample subfactors: sale of a license; incorporation in USSR State Standards. Maximum point value: 50. 4) Other forms of implementation. Sample subfactors: scientific monograph written; report delivered at all-union conference. Maximum point value: 40. Values for each factor are weighted and combined to yield a single integrated value. This value can then be divided by the cost of the research project, so that different projects can be compared not only in terms of absolute values, but in value per unit expenditure.

P1152(25/89)* Il'in YeA, Kaplanskiy AS, Savina YeA.

Rat experiments on COSMOS biosatellites: Morphological and biochemical research.

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina.

23(4): 4-9; 1989.

[63 references; 27 in English]

Space Biology and Medicine; Biochemistry, Morphology; Adaptation; Endocrinology; Hematology; Metabolism; Musculoskeletal System; Cardiovascular and Respiratory Systems; Gravitational Biology

Rats

Space Flight, COSMOS Biosatellites

Abstract: This paper reviews the morphological and biochemical results of rat experiments on COSMOS biosatellites, for flights lasting from 5-7 to 18-22 days. The short-term flight experiments demonstrated that signs of structural and metabolic restructuring occurs, even in the initial stage of adaptation to weightlessness. These changes affect the same systems that are altered during longer flights, with effects generally increasing with increasing flight durations.

One of the major systems affected by space flight is the musculoskeletal system. Changes here include decreased muscle mass, especially in antigravity muscles, and changes in muscle fibers, especially those with oxidative type metabolism. In a number of instances, e.g., the soleus muscle, atrophy is combined with dystrophic and destructive changes, including complete disintegration of the contractile apparatus in individual fibers. Muscle metabolism is also significantly affected, as shown by accumulation of excess glycogen and lipids in the muscles and decrease in ATPase myosin activity. All these changes lead to decreased rate and strength of contraction. Concomitant restructuring has also been noted in neuromuscular synapses, as have metabolic shifts (decreased protein and RNA) in motor neurons of the lumbar enlargement of the spinal cord and afferent neurons of spinal ganglia. These changes, involving decrease in muscle energy utilization and oxygen requirements, are accompanied by lowered blood supply (30% decrease in functioning capillaries in the gastrocnemius muscle in rats exposed to space).

Bone changes include: inhibited bone growth, delay in periosteal neoformation of bone tissue, development of osteoporosis of the spongy bone and, to a lesser extent, compact substance of the long tubular bones, and redistribution of minerals within a single bone. Histomorphologic analysis revealed that these phenomena are associated with inhibited neogenesis of bone tissue due to decreased number and activity of osteoblasts, and also enhanced resorption, as indicated by increased numbers of osteoclasts. These results are paralleled by biochemical data indicating depression of activity of alkaline phosphatases and enhanced activity of acid phosphatases in bones in rats exposed to microgravity. Most pronounced in the tubular bones, all these changes are associated with decreased bone strength. There is no doubt that endocrine glands participate in changes occurring in bone. In weightlessness, liberation of growth hormone from somatrophs is partially or completely blocked. In the thyroids of flight rats, the number and functional activity of C-cells that secrete calcitonin decreases. In the parathyroid, parathyrocytes (the producers of parathyroid hormone) are activated. The protein-calcium casts frequently found in the renal tubules of flight animals can be considered a side affect of bone demineralization and increased calcium excretion.

Blood changes that serve to normalize the relationship between blood cells and plasma, which has been disrupted by fluid loss due to decreased muscle capillaries, include inhibition of erythroid hemopoiesis, enhanced hemolysis of erythrocytes, and decreased erythrocyte lifetime. Bone marrow of flight animals contains a large number of abnormal megakaryocytes, testifying to disruption of thrombocytopoiesis, which can in turn lead to clotting disorders.

Decreased circulating blood volume and musculoskeletal loading decrease the loading on the heart, leading to atrophic processes. Evidence for this includes decreased activity of ATPase myosin and concentration of sarcoplasmic proteins in the myocardium, partial lysis of the myofibrillar apparatus, decreases in number and size of mitochondria and in relative size of the sarcoplasmic reticulum in cardiomyocytes. The aforementioned metabolic and structural shifts are thought to be the cause of the cardiac deconditioning occurring in weightlessness.

It is difficult to differentiate between changes attributable to weightlessness and those occurring as a result of acute gravitational stress after landing. It does appear likely that the functional activity of the hypothalamus-pituitary system decreases in weightlessness. This conclusion is based on significant decreases in Herring bodies in the anterior lobe of the pituitary. At the same time, examination of gonadotrophs and testes reveal no disruption of the gonadotropic function of the adenohypophysis.

It is very difficult to draw conclusions about effects of weightlessness on the adrenal cortex by direct study of adrenocorticocytes after landing, since the effects of acute gravitational stress may completely mask them. Thus, data on this system is obtained indirectly from studying lymphoid organs which are the targets for corticosteroids produced by the adrenal cortex in response to ACTH. Such studies have revealed that the weight of lymphoid organs is depressed immediately postflight, involution of the thymus occurs, and hypoplasia of lymphoid tissue can be observed in the spleen and lymphatic organs. Such changes can result either from stress or from inhibition of lymphocyte proliferation, which has been noted frequently and which may be associated with decreased growth hormone in blood.

Rats exposed to weightlessness display hypersecretory activity of the stomach and some decrease in the functional activity of the exocrine portion of the pancreas (decreased activity of amylase, trypsin, and lipase). Compensatory changes in the small intestine include activation of lipase, carbohydrase, and membrane digestion utilizing peptidase.

The authors summarize by concluding that the majority of structural and metabolic changes occurring in weightlessness are directly or indirectly related to decreases in functional loading on major physiological systems. The effect of this is deconditioning leading to decreased tolerance for all sorts of loadings, including reexposure to gravity. This leads to development of gravitational stress symptoms after reentry, the severity of which depends on the degree of adaptation to microgravity, which in turn depends on flight duration.

Use of artificial gravity on COSMOS satellites prevented the development of general and many specific structural/functional changes typically occurring in space. Gamma irradiation did not interact with weightlessness to enhance the effects of either factor, with the exception of blood system effects.

MONOGRAPH:

M149 (25/89) Malkin VB, Kosmolinskiy FP, Kuznets Yel (editors).
 Chelovek i Kosmos: Idei K.E. Tsiolkovskogo i ikh razvitiye v sovremennoy biomeditsine. Trudy XXII Chteniy, posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idej K.E. Tsiolkovskogo (Kaluga, 15-18 sentyabrya 1987). Человек и Космос Идеи К.Э. Циолковского и их Развитие в современной биомедицине. Труды XXII Чтений; посвященных разработке научного наследия и развитию идей К.Э. Циолковского (Калуга; 15-18 сентября 1987)

Man and space: The Ideas of K.E. Tsiolkovskiy and their development in modern biomedicine. Works from the XXII lecture series devoted to development of the scientific heritage and development of the ideas of K.E. Tsiolkovskiy (Kaluga, 15-18 September, 1987) Moscow: Soviet Academy of Sciences; 1988.

[72 pages; 6 tables; 2 figures]

Affiliation (monograph): The Commission on Development of the Scientific Heritage of K.E. Tsiolkovskiy, USSR Academy of Sciences; K.E. Tsiolkovskiy State Museum of the History of Cosmonautics

KEY WORDS: Space Biology and Medicine; Exobiology; Botany; Neurophysiology; Human Performance; Psychology; Operational Medicine; Space Flight; Thermal Status; Immunology; Botany; Pharmacology; Immersion; Life Support Systems

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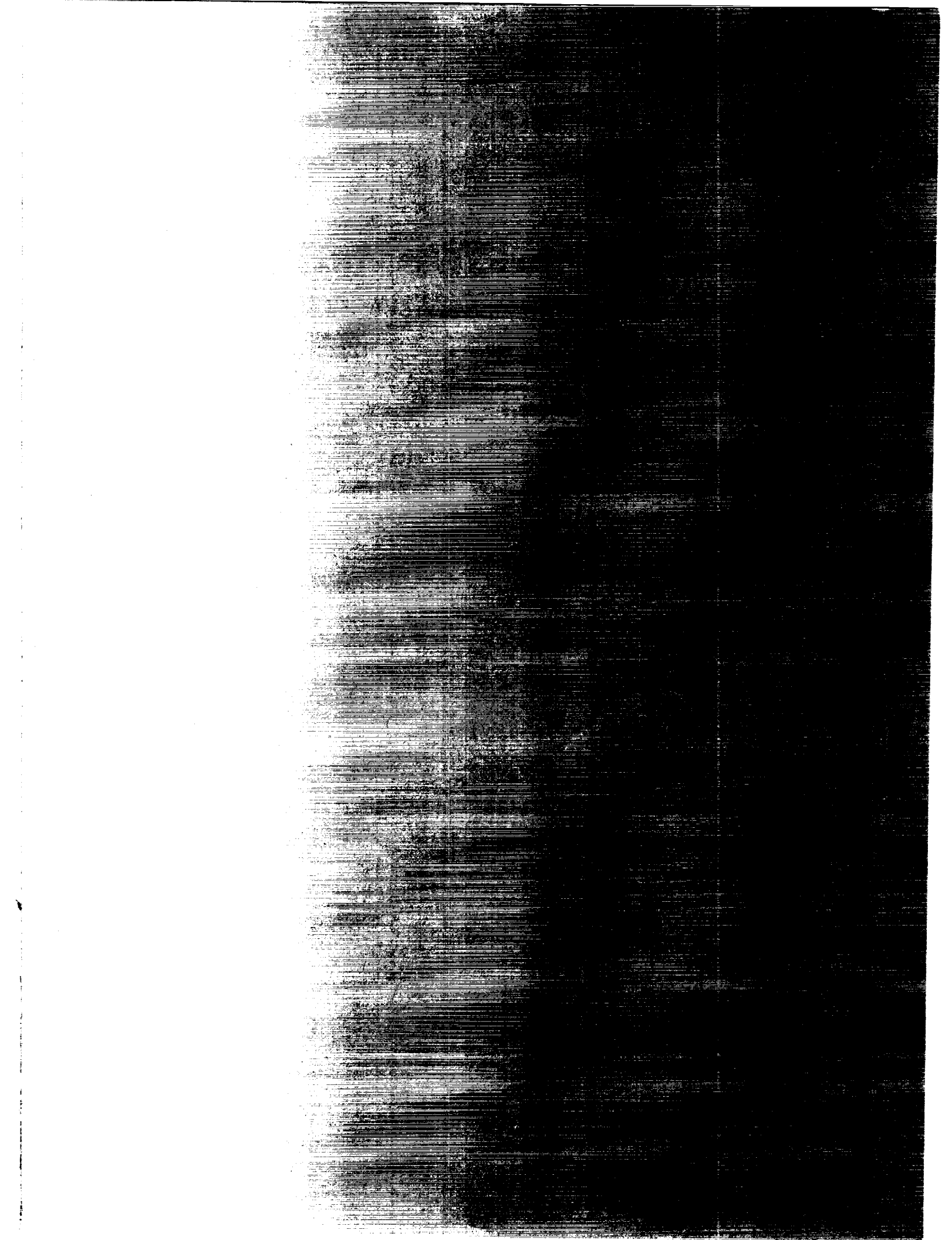
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